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ROENTGEN DIAGNOSIS DURING THE COURSE OF ROENTGEN THERAPY OF EPITHELIOMAS OF THE LARYNX AND HYPOPHARYNX*

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THE systematic use of roentgenography of the cervical region is of the greatest importance in the diagnosis of epitheliomas of the larynx and of the hypopharynx and also in the study of the effect of roentgen therapy on these tumors.

Before presenting roentgenograms of epitheliomas which were followed roentgenographically from their inception until their disappearance, it is essential to study the normal appearance of this region. The material will be given in the following order:

I. A description of the roentgenographic appearance of the normal larynx and hypopharynx.

II. A statement of the principal reasons which led us to consider the roentgenologic study necessary.

III. A description of the changes in the roentgen appearance of the larynx and hypopharynx which occur when an epithelioma develops.

IV. A comparison of the roentgen appearance of the cancerous larynx and hypopharynx before, during and after roentgen therapy.

I. THE ROENTGEN APPEARANCE OF THE NORMAL LARYNX AND HYPOPHARYNX

The normal appearance of the larynx and hypopharynx is characterized by the existence of very clear shadows and transparencies having well-defined contours, which are very easily demonstrated. The technique used is 60–80 kv., 80 cm. distance, 30–40 ma., and $\frac{1}{3}$ second. This is sufficient in most cases when double intensifying screens are used; $1\frac{1}{4}$ seconds is necessary without screens. The patient lies in the recumbent position, neck extended. The head is thus held well back so that the hyoid bone does not overlap the lower jaw; the direction of the rays is horizontal.

Four essential points are to be noted in the study of the normal larynx and hypopharynx: the framework, the shadows, the transparencies, and the relations of the various parts to each other.

(1) *The semi-rigid osteocartilaginous framework* (Figs. 1, 2, and 3) is formed by: the bodies of the second to the seventh cervical vertebrae (G); the horizontal ramus of the mandible (A); the hyoid bone (B) with its large cornuae (B^1); the thyroid cartilage (C) with its superior wings (C^1), its superior margin (C^2), posterior margin (C^3), and inferior (C^4) margin, and its inferior wings (C^5); the arytenoid cartilages (D); the cricoid cartilage (E), and its cusp (E^1); the tracheal rings below the larynx (F).

On this osteocartilaginous framework are

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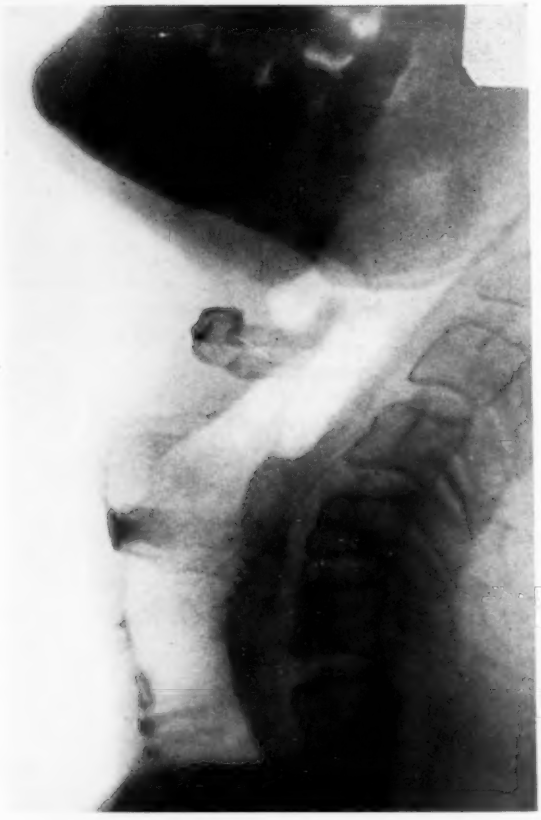


FIG. 1. Normal larynx and hypopharynx.

superimposed shadows cast by muscles and ligaments. These shadows are separated into anterior and posterior parts by a roentgenographically light zone.

(2) *The soft tissue shadows* (Figs. 1, 2, 3, 4 and 5). For convenience in the diagnosis of tumors, this region may be divided into three portions: the suprahyoid, thyrohyoid and thyrocricoid regions.

The suprahyoid region: This is limited above by a line passing 1.5 cm. above the inferior border of the horizontal ramus of the mandible and traversing the second cervical vertebra, 1 cm. above the second-third intervertebral space; below by the hyoid bone which usually corresponds to the third intervertebral space; behind by the second cervical (lower third) and third cervical vertebra. In front of the transparency is the base of the tongue (*f*) which forms the anterosuperior wall of the hypopharynx. In addition, the suprahyoid portion of the epiglottis (*g*) is also seen. The base of the tongue is united to the epiglottis by the glossoepiglottic fold (*h*), whose curve, concavity upwards, is always visible. Behind the transparency is the posterior pharyngeal wall (*i*) and the insertion of the posterior palatine folds (*j*).

The thyrohyoid portion: This is limited above by the hyoid bone; below by the superior border of the thyroid cartilage which corresponds generally to the fourth-fifth intervertebral space, behind by the fourth cervical vertebra. In front of the transparency is the middle or thyrohyoid portion of the epiglottis (g^1); on the anterior surface of the epiglottis a zone corresponding to the cellular tissue filling the pre-

FIG. 2. Normal larynx and hypopharynx.

epiglottic space (g^2); behind the epiglottis are found the aryteno-epiglottic ligaments; their posterior margin always visible (k) is situated between the lateral portions of the epiglottis and the arytenoid cartilages. At the level of the hyoid bone is sometimes seen the transverse projection of the pharyngo-epiglottic ligaments.

Behind the transparent area is found the posterior pharyngeal wall (i') and the superior thyroid cornuae (C^1) which are projected tangentially to the anterior surface of the fourth cervical vertebra.

The thyrocricoid portion: This is limited above by the superior border of the thyroid cartilage, below by the inferior border of the cricoid cartilage and behind by the fifth and sixth cervical vertebrae. Anterior to the transparency is the thyroid portion of the epiglottis (g^3) or the thyro-epiglottic ligament, which is attached to the anterior border of the thyroid cartilage. In front of the epiglottis is a cellular pre-epiglottic layer which is a continuation of the pre-epiglottic space situated in the thyrohyoid portion (g^2). On the thick portion of the thyroid cartilage, a little below the insertion of the thyro-epiglottic ligament, are inserted the two ventricular bands (v) and several millimeters farther below, are the two vocal cords (v^1). Still farther down are also found the inferior portion of the thyroid cartilage, the anterior thyrocricoid space, the anterior border of the cricoid cartilage (E), and the anterior border of the tracheal rings (F).

Behind the transparency are the posterior borders of the two thyroid wings (C^3), with the inferior cornuae (C^5), the

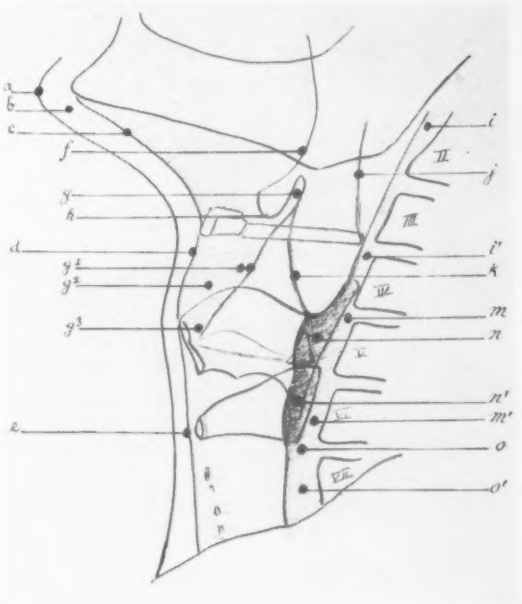


FIG. 4. Normal larynx and hypopharynx. Soft tissue shadows. *a*—skin. *b*—subcutaneous tissue. *c*, *d*, *e*—Middle cervical aponeurosis covering the muscular planes. *f*—Base of the tongue. *g*—Epiglottis. g^1—Posterior aspect of the epiglottis, thyroid portion. g^2—Cellular tissue filling the pre-epiglottic space. g^3—Thyroid portion of the epiglottis. *h*—Glosso-epiglottic ligament. *i*–*i'*—Posterior pharyngeal wall. *j*—Inferior portion of the posterior wall. *k*—Aryteno-epiglottic ligament. *m*–*m'*—Vertebro-laryngeal space. *n*–*n'*—Posterior opaque space. *o*—Esophageal opening. *o'*—Esophagus.

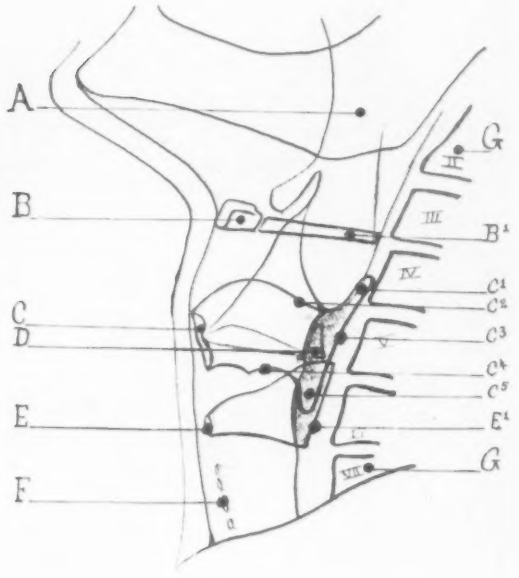


FIG. 3. Normal larynx and hypopharynx. Osteo-cartilaginous framework. *A*—Mandible. *B*—Hyoid bone. B^1—Great cornuae of the hyoid. *C*—Thyroid cartilage. C^1—Superior cornuae of the thyroid cartilage. C^2—Superior border of the thyroid cartilage. C^3—Posterior border of the thyroid cartilage. C^4—Inferior border of the thyroid cartilage. C^5—Inferior cornuae of the thyroid cartilage. *D*—Arytenoid. *E*—Cricoid. E^1—Cricoid cusp. *F*—Tracheal rings. *G*—Cervical vertebrae (II–VII).

Behind the transparency are the posterior borders of the two thyroid wings (C^3), with the inferior cornuae (C^5), the

two arytenoid cartilages (*D*) (on which are inserted the two ventricular bands (*v*) and a little below the two cords (v^1)) and the cricoid cusp (E^1). These different posterior borders are nearly tangential to the an-

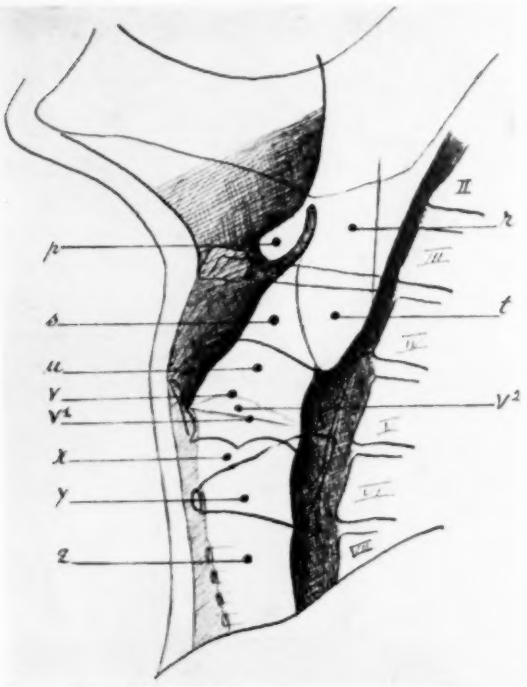


FIG. 5. Normal larynx and hypopharynx. Radiotransparencies. *p*—Epiglottic vallecula. *r*—Beginning of the laryngeal and pharyngeal vestibules. *s*—Laryngeal vestibule. *t*—Pharyngeal vestibule. *u*—Superior laryngeal clear space. *v*—Ventricular band. v^1—Vocal cord. v^2—Ventricle of Morgagni. *x*—Subglottic clear space. *y*—Cricoid clear space. *z*—Tracheal clear space.

terior surface of the fifth and sixth cervical vertebrae and constitute roentgenographically a part of the vertebro-laryngeal space (*m–m'*). This space, situated between the vertebral column and the larynx, is at most a few millimeters in width and is formed by the pharyngeal muscles and aponeuroses, covered by pharyngeal mucosa, posteriorly and anteriorly. The anterior pharyngeal mucosa covers the intercricoarytenoid ligaments above and the posterior surface of the cricoid at the level of the cusp below.

The vertebro-laryngeal space is included within a denser shadow which is called "the posterior opaque space" (*n–n'*). This corresponds to the thickening of the thyroid laminae in their posterior portions, i.e., in the region of the insertions of the inferior and superior cornuae, as well as to the superimposition of the arytenoids and the thyroid laminae, and finally to the inferior segments of the pharyngo-laryngeal groove or the piriform sinus. In this region the alimentary canal is more important laterally than medially; it is especially latero-arytenoid and latero-cricoid. The anterior portion of these very opaque laryngo-pharyngeal grooves is in one place made up of the arytenoids and in the other, of the cricoid, forming thus two slight curves somewhat concave behind. This posterior opaque space is 5 cm. in height and normally 7–10 mm. in width. It is a little larger above, smaller below. Normally it is larger than the vertebro-laryngeal space.

Lower still posteriorly is the opening of the esophagus (*o*) roughly on a level with the inferior surface of the cricoid which corresponds to the sixth–seventh intervertebral space; and still lower the esophagus (*o'*); the thickness of the esophageal shadow is about equal to the width of the shadow of the lateral cricoid portion of the pharynx (*n–n'*).

(3) *The Radiotransparent Portions* (Figs. 1, 2, 3, 4, and 5).

The suprahyoid portion: Between the epiglottis (*g*) and the base of the tongue (*f*) there is a transparency of which the lower concave border is formed by the glosso-epiglottic folds; this is the vallecular lumen (*p*). Between the base of the tongue and the epiglottis on the one hand, and the posterior pharyngeal wall (*i*) on the other, is a transparency 3 cm. in depth and 3 cm. in height which constitutes the beginning of the laryngeal and pharyngeal vestibules (*r*).

The thyrohyoid portion: Between the anterior or epiglottic wall (g^1), and the posterior wall of the pharynx (*i'*) there is a rectangular clear space which constitutes the inferior part of the laryngeal and

pharyngeal vestibule. The laryngeal vestibule (*s*) is limited in front by the epiglottis, behind by the posterior border of the aryteno-epiglottic ligament (*k*). The pharyngeal vestibule (*t*) is limited in front by the same ligament (*k*) and behind by the posterior pharyngeal wall (*i'*); it appears in the form of a funnel and is more radiotransparent than the laryngeal vestibule.

The thyrocricoid portion: Through all of its extent from the superior border of the thyroid cartilage to the inferior border of the cricoid and between the anterior and posterior walls, there is a very clear cylindrical zone (*u*, *x*, *y*) about 5 cm. in height by 2.5 to 3 cm. in width which constitutes the laryngeal lumen. It is not uniform. At the level of and above the ventricular band (*v*), and at the level of and below the cord (v^1), there is some decrease in transparency due to the thickness of the muscles. Between the cords and the bands the transparency is increased due to the presence of a cavity, the ventricle of Morgagni (v^2). Five millimeters below the cords there is another increase in the transparency—the subglottic region (*x*). At the level of the inferior part of the thyroid cartilage there is sometimes a superimposition of this cartilage on the superior border of the cricoid causing a diminution in transparency. The laryngeal lumen is continued below as the cricoid lumen (*y*) and the tracheal space (*z*) having the same size.

(4) *The Relationships of the Various Segments of the Larynx and Hypopharynx.* These organs, taken as a whole, are more or less movable; the thyroid, cricoid and arytenoid cartilages are relatively united and cannot very well change their interrelationships. The other segments of the larynx and hypopharynx can, in pathological conditions, vary in their relations and size, particularly the hyomandibular, hyothyroid and pre-epiglottic spaces which can vary materially in shape and size. The posterior opaque space varies considerably in appearance. The vertebro-laryngeal space, the size of which varies from 1 to 4 mm., may reach 20 to 30 mm. and appear elongated, conical or hemispherical. The variations in the relations of the segments and in the size of the interosseous, intercartilaginous or interligamentous spaces are very important in the diagnosis of tumors of these regions.

II. THE REASONS FOR THE NECESSITY OF ROENTGENOGRAPHIC STUDY

It is evident that roentgen examination is important at the onset of the lesion (that is, before roentgen therapy) as well as during and after therapy.

(*A*) Before roentgen therapy.

(*a*) Roentgen examination is necessary for the early diagnosis of cases which the laryngologist would easily recognize were he called to examine the patient at the beginning of the development of the epithelioma. It is rare that the advice of the laryngologist is asked at this time because cancers of the larynx and hypopharynx are usually not painful for a year, sometimes even two years, because they manifest their presence (except in carcinoma of the vocal cord) only by intermittent symptoms such as slight dysphonia and slowness in swallowing. They definitely indicate their presence and attract attention when the late symptoms appear, as, for example, dyspnea, aphonia, dysphagia, otalgia, or cephalalgia, or when there develop carotid, supraclavicular, or mastoid nodes. Also, the nodes may have at some time been operated on before it has been definitely decided whether a primary lesion of the neighboring mucosa exists. The laryngeal or pharyngeal symptoms are sometimes so slight that twelve to eighteen months may elapse between the operation on the nodes and the appearance of the first objective symptoms pointing to epithelioma of the laryngeal or pharyngeal passages. The roentgenogram demonstrates such tumors early.

(*b*) Roentgen diagnosis is necessary in particularly difficult cases. Epitheliomas of the ventricle of Morgagni, of the pre-epiglottic thyrohyoid space, at the base of the pharyngo-laryngeal groove, of the mucosa of the posterior portion of the cricoid, of

the posteroinferior wall of the pharynx, and of the esophageal opening, can be discovered early only by experienced laryngologists. The lesions often remain unrecognized for a long while and sometimes can only be diagnosed by the roentgenogram.

(*c*) Roentgen studies are necessary to determine whether or not a tumor is suitable for roentgen therapy. The extent of the lesion, and particularly the determination of its lower border, its invasion of the cartilage, whether it is fungating or infiltrating, and its probable point of origin can be determined by means of the roentgenogram. It is thus possible to decide whether to treat the case by roentgen therapy alone or in combination with surgery.

(*B*) During roentgen therapy.

The appearance of changes in the epithelioma and its involution are easily followed by roentgenography, sometimes before changes are seen with the usual "mirror" examination. In the same way an excess of the daily dosage of radiation is manifested by small local edemas either in the interior of the tumor itself, or in the submucous cellular tissue. The finding of the edema demonstrable by roentgenography is one of the aids in determining whether the treatment should be given more rapidly or more slowly, depending upon whether the edema follows or precedes the neoplastic degeneration.

(*C*) After roentgen therapy.

Roentgenographic control permits a determination as to whether the lesion in the larynx and hypopharynx has disappeared, whether the cartilages are invaded and are actually necrotic. The differential diagnosis between a recurrence of the tumor and a

FIGS. 6 and 7. Case 1. Roentgenogram and diagram showing carcinoma of false cord; extension to laryngeal cavity and base of epiglottis.

late necrosis is also better made from a roentgenographic than from a clinical examination.

III. THE CHANGES IN THE ROENTGEN APPEARANCE OF THE LARYNX AND HYPOPHARYNX WHEN AN EPITHELIOMA DEVELOPS

These changes roentgenographically are due to:

1. The projection of a very dense shadow onto a normally clear transparent space, without the distortion of the normal segments and spaces. This is the simplest diagnostic point to indicate the presence of a fungating tumor.

2. Distortion of the normal segments and spaces. This is a complicated case of an infiltrating tumor or a simple case of an epithelioma which has attained considerable size.

The projection of such shadows into the normal radiotransparent spaces and distortion of the segments of the larynx and hypopharynx are easily seen on the roentgenograms as shown by the following:

Epitheliomas of the Larynx

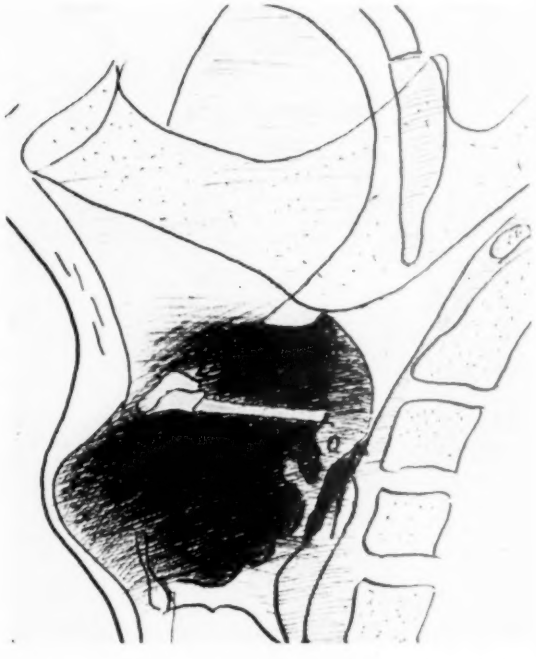
CASE I (Gr.) (Figs. 6 and 7) shows a dense shadow substituted for the normally clear laryngeal space. This shadow is produced by an epithelioma* having its origin at the level of the ventricular band and having invaded secondarily the subhyoid portion of the epiglottis, the pre-epiglottic space and the retro-epiglottic transparent spaces. It is not seen below the inferior border of the thyroid cartilage. The patient was operated on for a phlegmon of the neck eight months before admission to our

* In all tumors presented here biopsies were possible and the diagnosis of epithelioma established by microscopic examination.

FIGS. 8 and 9. Case II. Roentgenogram and drawing showing carcinoma of ventricular cavity. Extension into laryngeal cavity and base of epiglottis.

service; seven months later, that is, one month before roentgen therapy, a second operation was performed to remove a large sequestrum from the thyroid cartilage. The cartilage was invaded long before the patient presented any subjective symptoms referable to the larynx or pharynx.

CASE II (Bul.) (Figs. 8 and 9) shows a shadow projecting into the larynx and occupying its anterior three-quarters at the level of the thyroid cartilage. The tumor arose at the level of the ventricle of Morgagni and extended through the entire larynx to the base of the epiglottis and to the pre-epiglottic region where it developed slowly before being noted within the larynx.

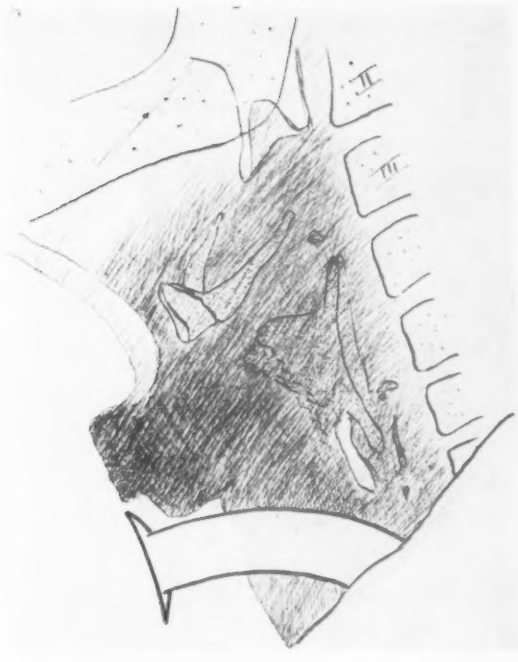


FIGS. 10 and 11. Case III. Roentgenogram and drawing showing carcinoma of the larynx having invaded the tissues anterior to it, through the epiglottis, through the base of the tongue, and forming a subcutaneous tumor mass.

CASE III (Gern.) (Figs. 10 and 11) shows a diffuse, vague mass obscuring the laryngeal and pharyngeal transparent spaces between the superior border of the epiglottis and the inferior border of the thyroid. Above, it invades the base of the tongue, below, the pre-epiglottic space, in front of which the subcutaneous cellular tissue is involved. The thyroid cartilage is destroyed. The origin was again in the ventricular band but the tumor became more extensive than in the preceding cases.

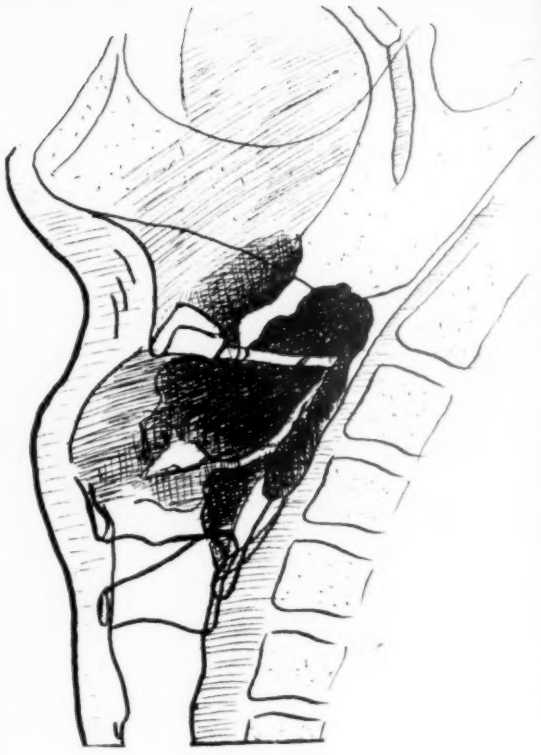
CASE IV (Lim.) (Figs. 12 and 13) shows an irregular shadow limited above by the mandible and below by a line passing horizontally through the esophageal opening; behind by the vertebral column; in front the tumor proliferates in the form of a mass which has destroyed the musculo-aponeurotic planes. The clear laryngeal and pharyngeal spaces are obliterated. Both cricoid and thyroid cartilages are in part destroyed. A tracheotomy was necessary eight months before the present examination. The epithelioma arose at the level of the vocal cord.

In the above cases of laryngeal epithelioma, the first examinations were made by us after the tumor had invaded all the endolarynx and taken on the characteristics of an extra-laryngeal or even a pharyngeal carcinoma. In Cases I, II and III the tumors were in the anterior part of the larynx; in Case IV the tumor occupied all the width of the neck, that is, there was

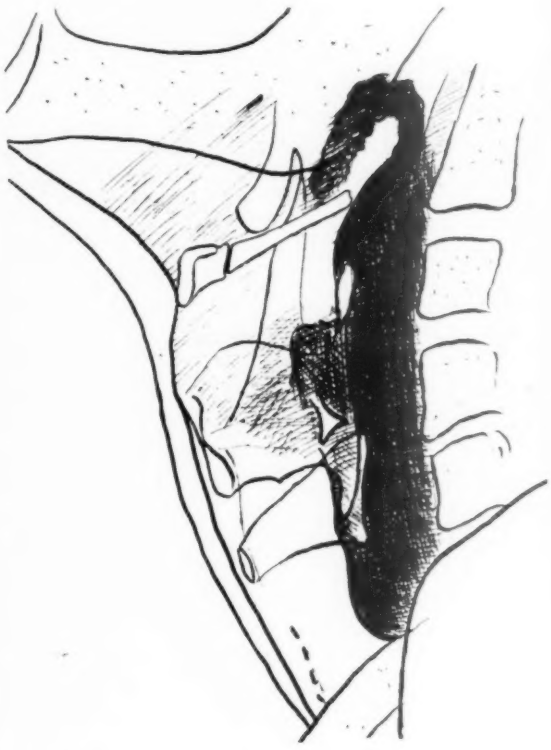


FIGS. 12 and 13. Case IV. Roentgenogram and drawing showing carcinoma of the larynx, starting from true cord; tracheotomy. The cancer advanced forward and upward, destroying the musculo-aponeurotic layers and forming a subcutaneous mass.

FIGS. 14 and 15. Case V. Roentgenogram and drawing showing carcinoma of the epiglottis, arytenoepiglottic fold and base of the tongue; destruction of the epiglottis.



FIGS. 16 and 17. Case VI. Roentgenogram and drawing showing carcinoma of the epiglottis, aryteno-glosso-pharyngo-epiglottic folds and base of the tongue.



FIGS. 18 and 19. Case VII. Roentgenogram and drawing showing carcinoma of the hypopharynx, mouth of the esophagus, with extension along the posterolateral wall of hypopharynx. Cartilages displaced forward with consequent increase in distance between larynx and cervical vertebrae.

complete secondary invasion of the hypopharynx.

Epitheliomas of the Hypopharynx

Case v (Mot.) (Figs. 14 and 15) shows a diffuse mass, in some places fungating, in other places infiltrating, which has invaded and destroyed the epiglottis, the aryteno-epiglottic, epiglottic, pharyngo-epiglottic, and aryteno-epiglottic ligaments, a part of the base of the tongue and the posterolateral pharyngeal wall, as well as a part of the cartilage. The growth of the tumor toward the pharyngolaryngeal groove is more marked than in the preceding case.

Case vii (Fourn.) (Figs. 18 and 19) shows a dense mass which does not protrude into the

Figs. 20 and 21. Case viii. Roentgenogram and drawing of non-infiltrating carcinoma of the true cord extending to subglottic space. The roentgenogram shows the inferior limit of the mass, impossible to recognize by clinical examination.

pharyngo-epiglottic and glosso-epiglottic ligaments, as well as the inferior portion of the base of the tongue. The tumor has invaded also the posterior soft tissues, and in particular the arytenoids; but the vertebro-laryngeal and the posterior opaque spaces remain intact, as does the anterior part of the larynx. The origin is apparently in the suprahyoid portion of the epiglottis; this is destroyed even in its thyrohyoid portion.

Case vi (Paw.) (Figs. 16 and 17) shows a diffuse mass, partly fungating, partly infiltrating, which has invaded the epiglottis, the glosso-laryngeal space but occupies the pharyngeal vestibule and widens the entire vertebro-laryngeal space by displacing the hyoid bone, the thyroid and cricoid cartilages 2.5 cm. away from the vertebrae. It is a tumor of the posterolateral pharyngeal wall, widest at the fifth and sixth cervical vertebrae. The tumor is 8–9 cm. in length and extends from the beginning of the esophagus to the superior margin of the hypopharynx. The diagnosis of this posterior tumor is facilitated by a recognition of the changes in the vertebro-laryngeal relationships.

IV. THE LARYNX AND HYPOPHARYNX STUDIED ROENTGENOGRAPHICALLY BEFORE, DURING AND AFTER ROENTGEN THERAPY

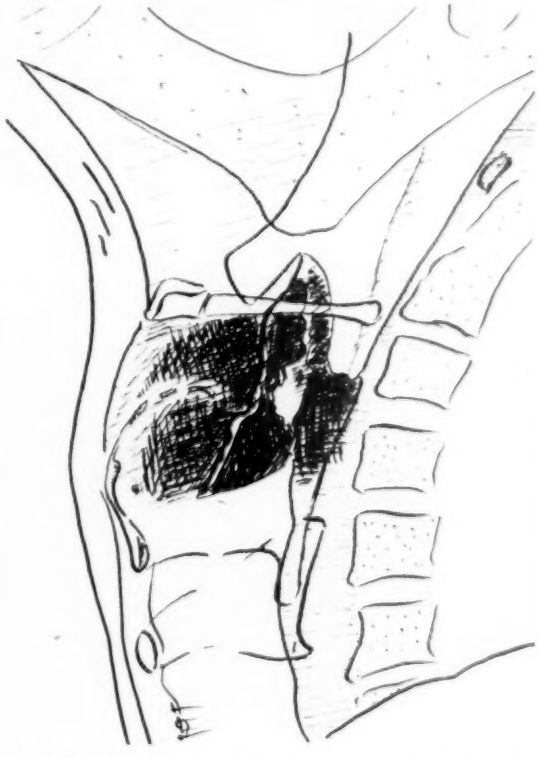
The exactness of the roentgen diagnosis can be controlled (along with histologic diagnosis) by a comparison of films taken before, during and after roentgen therapy.

Epitheliomas of the Larynx

CASE VIII (Blem.) (Figs. 20, 21 and 22) shows a fungating tumor, seen as a very dense shadow projected onto a clear space without deforming the segments or the normal spaces. The diagnosis is simple. There is an endolaryngeal tumor obscuring the ventricular band, the ventricular cavity, the cord and the anterior part of the subglottic region of the tongue. This tumor, the origin of which was on the anterior part of the cord, developed in part above it and somewhat behind, and in part below the cord and more in front; by mirror examination the lower limit of the tumor could not be determined.

This long-standing tumor caused not only dyspnea but a circulatory embarrassment which resulted in edema of the vertebro-laryngeal space. The displacement forward of the thyroid and cricoid cartilages was in this case not due to

FIG. 22. Case VIII. Roentgenogram showing the same case twenty-five days after beginning of roentgen therapy.



FIGS. 23 and 24. Case IX. Roentgenogram and drawing showing carcinoma of the larynx, ventricle of Morgagni, and false vocal cord, and invasion of pre-epiglottic space.

Fig. 25. Case IX. One month later.

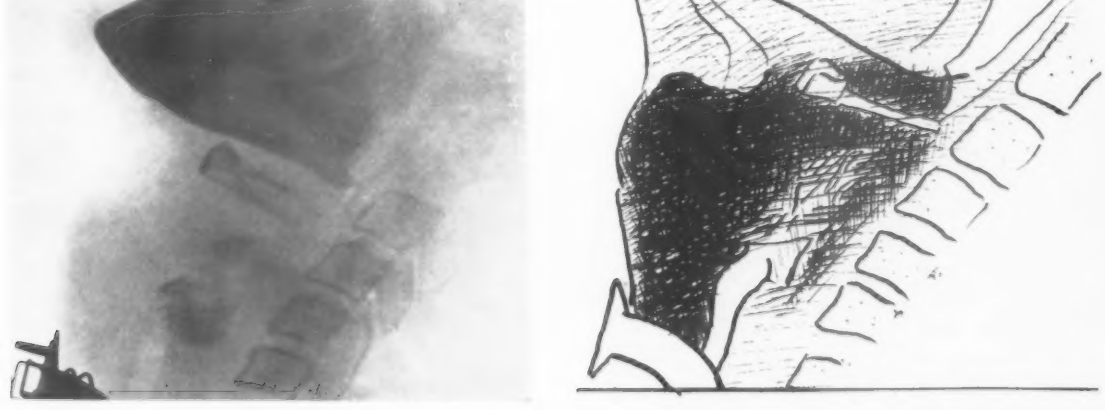
the tumor itself. Figure 22 taken on the twenty-fifth day after the beginning of roentgen therapy shows a reduction in the volume of the tumor during the course of treatment. Malignant tumors are the only ones which respond so rapidly to irradiation.

Case IX (Mer.) (Figs. 23, 24 and 25) shows an infiltrating tumor invading the epiglottis, the aryteno-epiglottic ligaments, and the pre-epiglottic region with edema of the vertebro-laryngeal space. The superior border of the thyroid cartilage is partially destroyed. The pre-epiglottic invasion displaces the epiglottis backwards. The tumor did not extend below the glottis. This is, therefore, an endolaryngeal tumor arising at the junction of the ventricular bands and the ventricle of Morgagni.

Figure 25, taken thirty days later, shows the epiglottis tending again to take its proper place, that is to say, to be in approximation with the anterior border of the thyroid cartilage because the pre-epiglottic tumor which caused the displacement of the epiglottis backwards was beginning to disappear. The invasion of the aryteno-epiglottic ligament has disappeared.

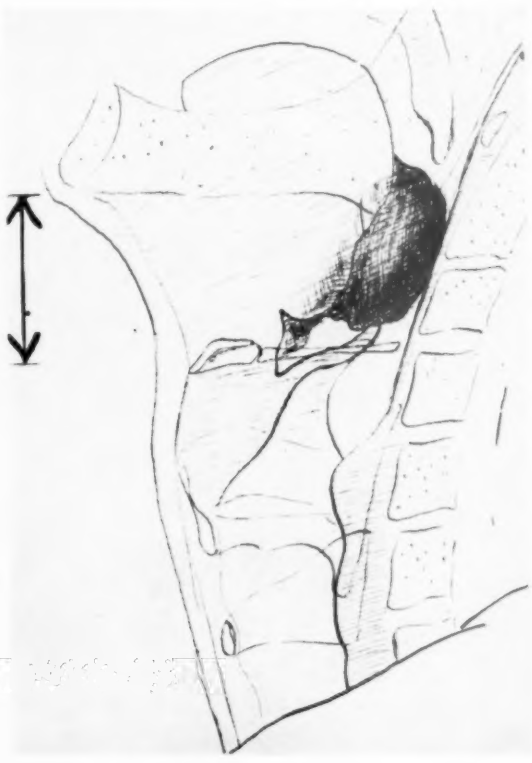
Case X (Baud.) (Figs. 26 and 27) shows an endolaryngeal and prelaryngeal mass with partial destruction of the cartilages. The entire laryngeal and pharyngeal clear spaces between the cricoid and the mandible have disappeared. The hyoid bone is displaced against the mandible. The tumor which was not superficially ulcerated had invaded the subcutaneous connective tissue. This patient had a laryngectomy twelve months ago for an epithelioma of the cords and the bands.

Figures 28 and 29 show the same larynx two years after roentgen therapy. The laryngeal



Figs. 26 and 27. Case X. Roentgenogram and drawing showing tumor of the true and false cords; post-operative recurrence after surgical intervention.

FIGS. 28 and 29. Case x. Two years after roentgen therapy. Return of normal and endolaryngeal lumen. The patient, however, could not have the tracheotomy tube removed, because of laryngectomy.



FIGS. 30 and 31. Case xi. Roentgenogram and drawing of carcinoma of the hypopharynx, base of the tongue, vallecula and lateral wall of the pharynx.

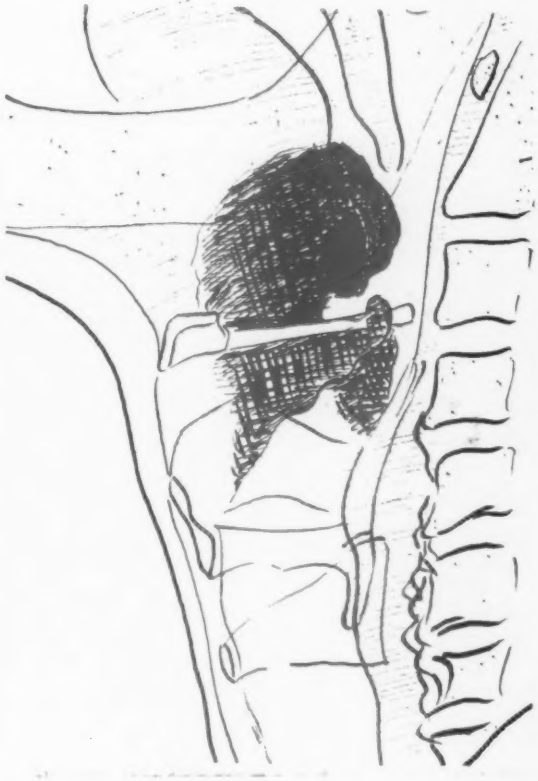
Fig. 32. Case xi. One year after roentgen therapy.

clear space is almost normal. Local cure appears certain. It was not possible to remove the cannula because of the previous surgical intervention. During the third year the patient showed signs of subclavicular and mediastinal adenopathy.

Epitheliomas of the Hypopharynx

We report below 2 cases of tumor of the anterior wall of the hypopharynx in its superior portion, at the level of the base of the tongue; 2 cases of epithelioma of the posterior wall of the hypopharynx in its superior portion; one case of tumor of the aryteno-epiglottic ligaments, and one case of tumor of the entire posterior pharyngeal wall.

Case xi (Berg.) (Figs. 30, 31 and 32) shows a tumor in the suprahyoid portion of the hypopharynx. It developed on the vertical portion of the tongue or at the base of the tongue. It is in apposition behind with the posterior pharyngeal wall, obscuring the clear space of the laryngeal and pharyngeal vestibules in their superior portions. The hyoid is displaced downwards, the epiglottis backwards, the latter touching the posterior pharyngeal wall. The tumor is in-



Figs. 33 and 34. Case xii. Roentgenogram and drawing of carcinoma of base of the tongue, epiglottis, vallecula, and aryteno-epiglottic folds.

filtrating the lateral pharyngeal wall and the corresponding vallecula.

Figure 32 shows a return to normal one year later, with disappearance of the tumor and a normal appearance of the clear suprahyoid region.

CASE XII (Col.) (Figs. 33,34 and 35) is that of a tumor occupying the entire base of the tongue, assuming in the tongue an ovoid shape; it has destroyed the suprahyoid portion of the epiglottis, invaded the valleculae and the infrahyoid portion of the epiglottis as well as the aryteno-epiglottic ligaments.

After two years the same patient (Fig. 35) no longer shows any trace of the original tumor. The base of the tongue, the epiglottis, and valleculae, all have normal contours; the suprahyoid portion of the epiglottis has disappeared.

CASE XIII (Bil.) (Figs. 36,37 and 38) is that of a tumor of the posterior wall of the hypopharynx in its suprahyoid portion; it corresponds to the angle of the mandible. In Figure 38 the disappearance of the tumor can be noted one month after the beginning of the treatment.

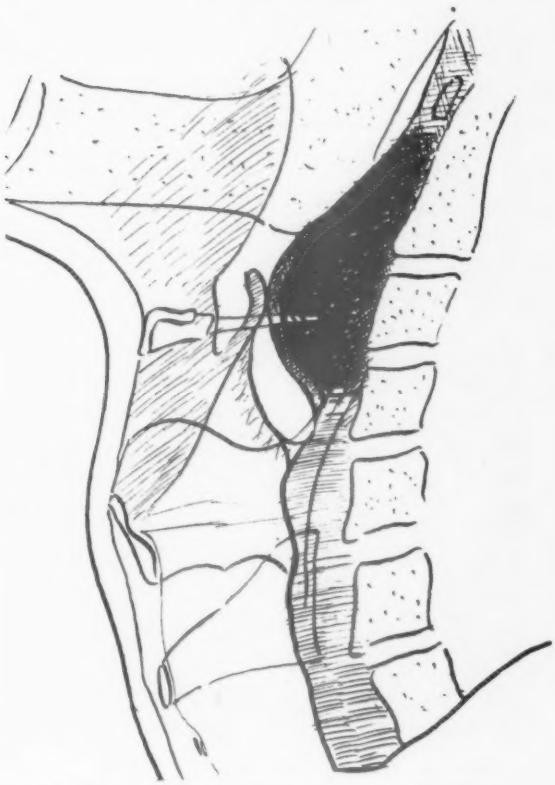
CASE XIV (Sch.) (Figs. 39, 40 and 41) is analogous to the preceding case. It is a tumor

FIG. 35. Case XII. Two years later.

FIGS. 36 and 37. Case XIII. Roentgenogram and drawing of carcinoma of posterosuperior wall of pharynx.

FIG. 38. Case XIII. One month later.

FIG. 41. Case XIV. One year later.



FIGS. 39 and 40. Case XIV. Roentgenogram and drawing of carcinoma of the posterior wall of pharynx.

of the posterior wall of the hypopharynx, but situated lower; the same region can be compared one year later.

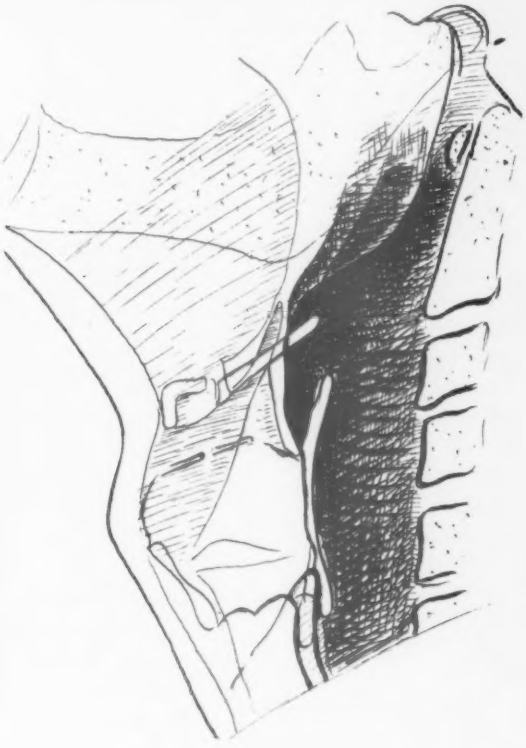
Case xv (Vuill.) (Figs. 42, 43 and 44) is a tumor which occupies the entire length of the aryteno-epiglottic ligaments (suprahyoid portion and thyrohyoid portion) before roentgen therapy and one year after roentgen therapy.

Case xvi (Ver.) (Figs. 45, 46, 47 and 48) shows a large epithelioma occupying a portion of the mesopharynx, the entire hypopharynx and the suprasternal esophagus.

The vertebro-laryngeal space which is normally not more than 4.0 mm. attains in this case a width of 2.0 to 2.5 cm. The tumor displaces forward the thyroid cartilage, the cricoid cartilage and the hyoid bone; the great cornuae are elevated. The "mirror" examination, very unsatisfactory because of the large mass of the neoplasm, showed only the superior pole of the tumor at the level of the epiglottis, resting against the tongue; it was impossible to obtain any idea of the extent of the lesion; the inferior limit could only be determined by roentgenography. Changes in the appearance of

Fig. 44. Case xv. One year later.

Figs. 42 and 43. Case xv. Roentgenogram and diagram showing tumor occupying the arytenoepiglottic fold.



Figs. 45 and 46. Case xvi. The larynx is pushed forward by a tumor mass evidenced by extremely marked shadow between the larynx and vertebrae (January, 1926).

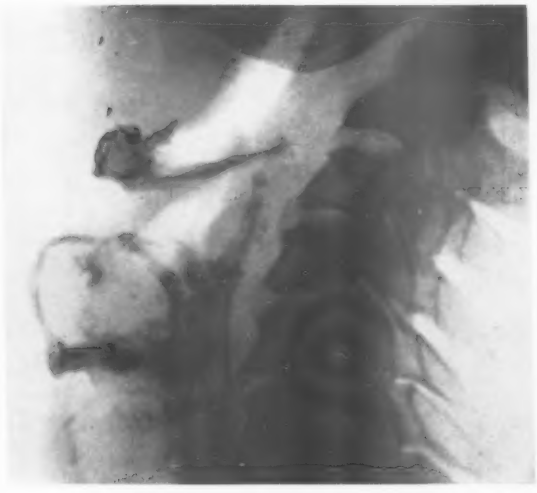


Fig. 47. Case xvi. One month later.

Fig. 48. Case xvi. 1929. The larynx is back in its normal position.

the thyroid cartilage seen here are due to decalcification, a frequent finding in very extensive tumors; the cartilages were not invaded.

Figure 47 shows a diminution in the size of the tumor one month after roentgen therapy was begun on January 25, 1926. At the same time that the tumor diminished in size, the hyoid bone and the thyroid and cricoid cartilages reapproached more closely the vertebral bodies; the vertebro-laryngeal space diminished.

Figure 48, taken at the end of 1929, shows the posterior extremities of the hyoid cornuae and the posterosuperior portions of the thyroid alae also projecting tangentially to the bodies of the vertebrae just as they appear in the normal larynx and hypopharynx. The patient was in excellent local and general health at the end of 1931.

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ROENTGEN THERAPY OF EPITHELIOMAS OF THE TONSILLAR REGION, HYPOPHARYNX AND LARYNX FROM 1920 TO 1926*

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I. ANATOMICAL-CLINICAL DEFINITION

AN ADEQUATE clinical observation of cancer, and especially of those cancers which concern us here, implies the necessity of repeated examinations during the course of treatment, as much from the point of view of changes in the appearance of the normal and neoplastic tissues under the influence of radiation as from the point of view of the accuracy of the topographic diagnosis.

When the therapy is used as it is here in cancers that are usually very widespread, the exact diagnosis of the point of origin of the neoplasm is often difficult to establish immediately; it is necessary to await the disappearance of the accompanying inflammation and the progressive diminution of the tumor masses which overrun and mask the initial lesion.

It may happen during the course of a treatment that the topographic diagnosis must be revised. It is found, for example, that extensive cancers beginning in the tonsillar region have been mistaken for cancers of the base of the tongue; that epitheliomas of the mucous membrane of the cheek, maxilla or palate have been mistaken in the beginning for cancers of the tonsillar region. In the same manner a tumor which totally obstructs the laryngeal vestibule is apt to be considered as having originated either in the larynx or pharynx; it is only during the course of treatment that the true primary lesions can be recognized and their true origin established.

The 46 epitheliomas of the tonsillar region which we have treated usually involved the tonsil and the tonsillar pillars, reaching (in more than half of the cases) the palate, the uvula and often the glossopharyngeal folds.[1] Frequently they came in contact with the epiglottis; often they extended to the tongue, the mucosa of the cheek, the gingival-jugular folds, the internal aspect of the inferior maxilla; more rarely the involvement reached the pterygomaxillary region causing trismus. In spite of their large size, they were usually only slightly painful.

The adenopathy, usually early, was constant, large, spherical in form, and somewhat indurated; it often remained movable for a long period over the deep structures. Its site corresponded to the angle of the maxilla; sometimes it descended along the carotid vessels and rarely reached the supraclavicular region; sometimes it was bilateral.

The 89 epitheliomas of the hypopharynx which we have treated, represented very dissimilar types. They originated between the postero-inferior edge of the base of the tongue and the mouth of the esophagus. Those of the superior and lateral edge of the epiglottis, of the lingual aspect of the epiglottis, of the aryteno-, pharyngo- and glosso-epiglottic folds were common. The cancers of the pharyngo-laryngeal canal (or pyriform sinus) and the glosso-epiglottic depressions (or valleculae) have been less numerous. Epitheliomas of the lateral and posterior walls of the pharynx were still less numerous, as were also epitheliomas of the anterior pharyngeal wall, i.e.,

[1] In the Curie Institute, epitheliomas of the tonsillar region of limited extension are treated preferably by radium therapy.

* Read by invitation at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N.J., Sept. 22–25, 1931.

the pharyngeal mucosa covering the interarytenoid surfaces and the cricoid plate. Epithelioma of the mouth of the esophagus has been rare.

Adenopathies were constantly observed, their site and size varying with the primary location, i.e., either carotid or supraclavicular, and sometimes mastoid. They were frequently infected and in 10 cases they had been removed or incised six months to one year before the diagnosis of their primary origin was established.

The 77 epitheliomas of the larynx which we have treated related especially to the vocal cord, to the subglottic region, to the ventricular band or to the ventricular cavity of Morgagni; they sometimes sprang from the anterior commissure or from the mucosa covering the inferior and laryngeal part of the epiglottis, or from the laryngeal mucosa of the arytenoids, also from the laryngeal slope of the interarytenoid space. These epitheliomas reacted very differently depending upon their point of origin, the degree of infiltration, the invasion of the cartilages and the superimposed infection. Most of these epitheliomas were very extensive and inoperable; others, previously operated upon, recurred; 8 were operable but seemed more amenable to irradiation than surgery.

The epitheliomas of the glottis were not accompanied by adenopathy, which we observed often in epitheliomas affecting the subglottic region. Adenopathies were the rule in epitheliomas of the ventricular bands and cavities, especially when the lesion had broken through the boundaries of the larynx and had assumed the characteristics of cancer of the hypopharynx.

Local recurrence, in case of failure of roentgen therapy, in the type of cancer which we have referred to, manifested itself at any period. It occurred most frequently between the sixth and twelfth months after the beginning of the treatment. In the cases treated between 1920 and 1926, when a patient remained without local signs of disease for fifteen months, we never observed a subsequent recurrence.

In the series of patients treated after 1926, we have observed two local recurrences which manifested themselves only at the end of the third year after the treatment; consequently we believe that a period of control of at least three years is necessary before a local cure can be accepted as probable.

On the other hand, we have observed in some of our patients locally cured, late distant metastases occurring during the third, fourth and fifth years. Therefore a period of control of five years is necessary before a total cure of the cancer process can be considered as probable.

In spite of this, in the attempt to demonstrate the unequal frequency of late metastases in the three varieties of epitheliomas under consideration, we have in Tables I, II and III, given first the results obtained after a period of control of two years. We have also given in the same tables and in the following tables, the statistics of patients living after three, five and eight years, statistics necessarily established on a diminishing number of patients treated.

TABLE I

EPITHELIOMAS OF THE TONSILLAR REGION TREATED BY X-RAYS 1920–1926

Years	Cases Treated	Locally Cured Two Years after Treatment	Dead after Two Years and Causes of Death	Symptom free at Beginning of 1931
1920	2	0		
1921	5	2		2
1922	3	1		1
1923	3	1	1 Pulmonary metastasis, dead the sixth year after treatment	0
1924	7	1		1
1925	13	1		1
1926	13	6		6
	46	12 (26%)	1	11 in 46 (23%)

II. STATISTICS AND CLASSIFICATION OF RESULTS

1. Tables I, II, III and IV show that 212 patients have been treated completely or have begun treatment by roentgen rays in my service at the Curie Institute from 1920 to 1926; 157 (74 per cent) died during the first two years following the treatment, either from extension of the primary lesion, or from early metastasis, sometimes from local or general post-roentgen accidents, and 55 (26 per cent) have been cured of the primary cancerous lesion.

These tables show, in addition, that the proportion of locally cured patients is essentially comparable in the three groups of epitheliomas under consideration, i.e.:

12 out of 46 (26 per cent) for cancers of the tonsillar region.

18 out of 89 (20 per cent) for cancers of the hypopharynx.

25 out of 77 (32 per cent) for cancers of the larynx.

None of these patients have presented local recurrence, but the proportion of late metastases occurring more than two years

TABLE II

EPITHELIOMAS OF THE LOWER PHARYNX TREATED BY X-RAYS 1920–1926

Years	Cases Treated	Locally Cured Two Years After Treatment	Dead After Two Years and Causes of Death	Symptom-free at Beginning of 1931
1920				
1921	7	1	1 Pulmonary metastasis, dead the sixth year after treatment	0
1922	11	4	3 (1) Prostatic hypertrophy, dead the fourth year after treatment; (2 and 3) Mediastinal and hepatic metastasis, dead the fifth year after treatment	1
1923	8	2	1 Abdominal metastasis, dead at beginning of the third year after treatment	1
1924	19	1		1
1925	24	5	2 Pulmonary and mediastinal metastasis, dead the third year after treatment	3
1926	20	5	2 Abdominal metastasis, dead the third year after treatment	3
	89	18 (20%)	9	9 in 89 (10%)
			8 in 18 (44%) dead of late metastasis 1 dead of intercurrent disease	

TABLE III

EPITHELIOMAS OF THE LARYNX TREATED BY X-RAYS 1920–1926

Years	Cases Treated	Locally Cured Two Years after Treatment	Dead after Two Years and Causes of Death	Symptom-free at Beginning of 1931
1920				
1921	8	4		4
1922	11	1	1 Cardiac accidents, dead the fourth year after treatment	0
1923	12	2		2
1924	12	3	2 (1) Tuberculosis, dead the third year after treatment (2) Thoracic metastasis, dead the third year after treatment	1
1925	17	6		6
1926	17	9		9
	77	25 (32%)	3	22 (28%)

TABLE IV

EPITHELIOMAS OF THE TONSILLAR REGION, HYPOPHARYNX AND LARYNX TREATED BY X-RAYS 1920–1926

Proportion of Thoracic or Abdominal Metastasis After More Than Two Years of Local Cure

	Cases Treated	Locally Cured Two Years after Treatment	Symptom-free at Beginning of 1931	Causes of Death after More Than Two Years	
				Intercurrent diseases	Thoracic or abdominal metastasis
Tonsillar region	46	12 (26%)	11 in 46 (23%)		1 in 12 (8%)
Hypopharynx	89	18 (20%)	9 in 89 (10%)	(1) Prostatic hypertrophy	8 in 18 (44%)
Larynx	77	25 (32%)	22 in 77 (28%)	(1) Tuberculosis (1) Cardiac accidents	1 in 25 (4%)
	212	55 (26%)	42 in 212 (20%)	3	10 in 55 (18%)

after treatment varies with the location:

1 out of 12 (8 per cent) for cancers of the tonsillar region.

8 out of 18 (44 per cent) for cancers of the hypopharynx.

1 out of 25 (4 per cent) for cancers of the larynx;

so that the proportion of those living after three years of control remains for the first and third group:

12 out of 46 (26 per cent);

25 out of 77 (32 per cent);

but the percentage diminishes in epitheliomas of the hypopharynx to:

13 out of 89 (14 per cent).

We have seen only one case of late pulmonary metastasis occurring during the sixth year after treatment in our epitheliomas of the tonsillar region, and one case of metastasis during the fourth year in our epitheliomas of the larynx. In spite of the constancy of glandular invasion in epithelioma of the tonsillar region and in spite of their large size, late distant metastasis, contrary to what one would expect, seemed little to be feared in this type of cancer.

In epitheliomas of the hypopharynx, out of 18 patients locally cured after two years, we have observed 8 cases of late metastasis (3 abdominal and 2 thoracic during the third year, 2 thoracic during the fifth year, 1 pulmonary during the sixth year). The results of treatment of epitheliomas of the hypopharynx, although as favorable from the standpoint of local cure as for epitheliomas of the tonsillar region and larynx, are uncertain because of the development of metastasis.

2. It can be seen from Table v that the results controlled to January, 1931, for treatments given during the period of seven years (from 1920 to 1926) have varied according to the years. In 1922 and 1924, the proportion of favorable results was very low—only 8 per cent of definite cures—whereas for the other five years the proportion of definite cures was 24 per cent (37 out of 149). This difference in results can be attributed partly to a variable proportion of favorable cases during these years (1921, for example), and partly to more or less marked differences in technique during the period of study which represented the first seven years.

3. Table vi shows that the permanence of percentage of results considered in consecutive years, differs depending upon the location of the lesion. In epitheliomas of the hypopharynx, the percentage of cures decreases progressively and falls to 0 after nine years. In epitheliomas of the tonsillar region and larynx, the percentage of cures is maintained in a relatively constant manner, regardless of whether the observation is made after two, six or nine years.

TABLE V

EPITHELIOMAS OF THE TONSILLAR REGION, HYPOPHARYNX AND LARYNX TREATED BY X-RAYS 1920–1926
Proportion of Survivals, by Years, at Beginning of 1931

Years	Cases Treated	Symptom-free at Beginning of 1931				Survival Period
		Tonsillar Region	Hypopharynx	Larynx	Total	
1920	2	0 out of 2			0	
1921	20	2 out of 5	0 out of 7	4 out of 8	6 (30%)	9 years
1922	25	1 out of 3	1 out of 11	0 out of 11	2 (8%)	8 years
1923	23	0 out of 3	1 out of 8	2 out of 12	3 (13%)	7 years
1924	38	1 out of 7	1 out of 19	1 out of 12	3 (8%)	6 years
1925	54	1 out of 13	3 out of 24	6 out of 17	10 (18%)	5 years
1926	50	6 out of 13	3 out of 20	9 out of 17	18 (36%)	4 years
	212	23%	10%	28%	42(20%)	4 to 9 years

In this table it may be seen that the proportion of cures controlled three years after treatment in the patients treated from 1920 to 1926, is 50 out of 212 (23 per cent). These can be divided as follows:

12 out of 46 (26 per cent) for epitheliomas of the tonsillar region.

13 out of 89 (14 per cent) for epitheliomas of the hypopharynx.

25 out of 77 (32 per cent) for epitheliomas of the larynx.

The proportion of cures controlled five years after treatment in the patients

TABLE VI

EPITHELIOMAS OF THE TONSILLAR REGION, HYPOPHARYNX AND LARYNX TREATED BY X-RAYS 1920–1926

Results of Roentgen Therapy at Beginning of 1931 After More Than:

	Two Years (Cases Treated 1920–1926)	Three Years (Cases Treated 1920–1926)	Four Years (Cases Treated 1920–1926)	Five Years (Cases Treated 1920–1925)	Six Years (Cases Treated 1920–1924)	Seven Years (Cases Treated 1920–1923)	Eight Years (Cases Treated 1920–1922)	Nine Years (Cases Treated 1920–1921)
Tonsillar region	12 in 46 (26%)	12 in 46 (26%)	12 in 46 (26%)	6 in 33 (18%)	5 in 20 (25%)	3 in 13 (23%)	3 in 10 (30%)	2 in 7 (28%)
Hypopharynx	18 in 89 (20%)	13 in 89 (14%)	12 in 89 (13%)	7 in 69 (10%)	4 in 45 (9%)	2 in 26 (7%)	1 in 18 (5%)	0 in 7
Larynx	25 in 77 (32%)	25 in 77 (32%)	22 in 77 (28%)	13 in 60 (21%)	7 in 43 (16%)	6 in 31 (19%)	4 in 19 (21%)	4 in 8 (50%)
	55 in 212 (26%)	50 in 212 (23%)	46 in 212 (21%)	26 in 162 (16%)	16 in 108 (14%)	11 in 70 (16%)	8 in 47 (17%)	6 in 22 (27%)

treated from 1920 to 1925 is 27 out of 162 (16 per cent), which may be divided as follows:

6 out of 33 (18 per cent) for epitheliomas of the tonsillar region.

8 out of 69 (11 per cent) for epitheliomas of the hypopharynx.

13 out of 60 (21 per cent) for epitheliomas of the larynx.

The proportion of cures controlled eight years after treatment in the patients treated from 1920 to 1922 is 8 out of 47 (17 per cent) which can be divided as follows:

3 out of 10 (30 per cent) for epitheliomas of the tonsillar region.

1 out of 18 (5 per cent) for epitheliomas of the hypopharynx.

4 out of 19 (21 per cent) for epitheliomas of the larynx.

4. Table VII shows that the proportion of females with epithelioma of the tonsillar region, hypopharynx and larynx, is small compared with the proportion of males affected by these lesions: out of 212 cases treated, 197 were males (93 per cent), and 15 were females (7 per cent). This table also shows that the cure of these epitheliomas is more easily accomplished in women than in men, since up to January 1, 1931, out of 15 women treated, 9 (60 per cent) are free of disease from four to nine years, whereas the proportion of men treated during the same period and free of symptoms at the same time (1931) is only 33 out of 197 (16 per cent).

TABLE VII

EPITHELIOMAS OF THE TONSILLAR REGION, HYPOPHARYNX AND LARYNX TREATED BY X-RAYS 1920–1926

Proportion of Survivals at Beginning of 1931, in Males and Females

	Cases Treated	Symptom-free at Beginning of 1931
Males	197 (93%)	33 (16%)
Females	15 (7%)	9 (60%)
	212	42 (20%)

5. Critique of Results. The epitheliomas of the tonsillar region, in spite of the very extensive development of the lesions in the primary growth and the invasion of lymphatic glands, have given us fairly good results during the years 1921 to 1926. But it is only since 1926 that the results of roentgen therapy alone have shown an appreciable improvement (46 per cent).

The cancers of the hypopharynx which we have treated were all inoperable; therefore none of those which were cured locally had been subjected to previous surgical intervention.

Among the epitheliomas of the larynx there were a variety situated in the cord, glottis or even subglottis, sometimes small, at other times reaching a considerable size; but in all instances they infiltrated the laryngeal muscles only slightly, leaving the organ fairly mobile. These epitheliomas are easily cured by irradiation and offer almost constant success to roentgen therapy. Surgery is also successful in a high proportion of this variety, but the conservation of the voice is less perfect after surgery than after radiotherapy. On the other hand, when roentgen therapy given in curative doses fails, future surgical intervention is rendered dangerous on account of the changes provoked in the tissues, while irradiation can be used without danger in a postoperative recurrence. The satisfactory results obtained in 1921 can be explained partly by the fact that in two patients with epithelioma of the cord without infiltration and without diminution of mobility of the larynx, there were contraindications to operation, one because the lesions were bilateral, having spread from the anterior commissure to the arytenoids, the other on account of obesity.

On the contrary, when a very small cancer of the vocal cord has caused fixation by infiltration of the muscles and if it has already reached the cartilages or provoked a perichondritis, and when histological examination shows a particularly resistant epithelioma, failure of roentgen therapy is the rule. If in such cases, as Hautant has practised several times, a resection of the infiltrated and infected areas adherent to the cartilage is performed (without pretending that the operative procedure removes the entire neoplasm) roentgen therapy can effect a definite disappearance of the neoplastic process. In several cases of cancer of the larynx treated in 1926, this combination of surgery and radiation was used, the result of which has been cure in 53 per cent.

Among the cases treated, there exists a certain number in which the site of origin is not in the vocal cord, but in the ventricular band. In epitheliomas of the band, although showing a marked degree of infiltration and infection and involvement of the cartilage, the histological form is generally much more favorable and roentgen therapy can effect a cure without recourse to surgery, which in tumors of marked radiosensitivity but equally marked tendency to diffusion, is apt to facilitate the dissemination of neoplastic cells.

Considering the large number of varieties and locations of epitheliomas of the hypopharynx and larynx, it is very difficult to decide which therapeutic method is to be applied. But it may be stated at present that for certain locations and certain states of development, roentgen therapy should accomplish almost unvarying success, whereas for other locations and other states of development, roentgen therapy, at least at present, yields no results. There are cases in which the association of surgery and irradiation or irradiation and surgery should be advantageous, but the rules for the selection of these cases are not definite.

The presence of very extensive adenopathy, sometimes subclavicular and retroclavicular, frequently infected and often bilateral, adds to the complexity of the problem. At any rate, the cure of unilateral adenopathy by roentgen therapy is relatively easy except in the cases where the lymphatic glands are the seat of an associated bacterial infection.

III. TECHNIQUE OF TREATMENT

1. *Total doses. Total duration of treatment. Number and surface area of fields. Focal distance.*

The epitheliomas of the tonsillar region in females which have been cured (4 out of 8 cases treated) have received cutaneous doses of 50, 69, 73 and 78 Holzknecht units (H), i.e., 5,000 r, 6,900 r, 7,300 r, and 7,800

r (International unit)[2] administered consecutively over periods of 17, 20, 41 and 29 days. In the cured males, the treatments have been 68, 78, 79 and 79 H, administered over periods of 37, 30, 34 and 40 days. In 3 other cases of cured males, very weak doses of roentgen rays (40 H in 14 days, 59 H in 83 days and 59 H in 50 days) had been supplemented with radium.

Doses of 100 to 120 H were frequently administered in 1923; we reached 150 and 160 H in 40 to 45 days during the year 1924; in 1926, we reached doses of 100 to 130 H in 30 to 50 days. These treatments with high doses did not give us any favorable results, except for one patient who, in 1923, received 150 H in 41 days, and was cured locally. During the fifth year, however, he developed radionecrosis of the inferior maxilla which culminated in elimination of a sequestrum followed by cicatrization. Some time later extensive pulmonary metastases appeared which caused death six years after treatment.

In all these cases, up to 1923, the fields have been 50 to 100 sq. cm.; later they were increased to 150 and even 200 sq. cm.; the focal distance has been from 40 to 50 cm.

The epitheliomas of the hypopharynx in females, cured in a proportion of 2 out of 4, have received in one case 46 H in 8 days with a field of 60 sq. cm., in the other case 77 H was administered in 30 days, with a slightly larger field.

In the males, the doses which have resulted in cures have been 60 H in 10 days, 66 H in 24 days, 71 H in 31 days, 75 H in 25 and 32 days; in 2 other cured cases, the doses were administered over very long periods: 74 H in 61 days and 81 H in 47 days. Treatment has been attempted with doses of 90, 100 and 105 H with no favorable results. The fields which until 1923 had been less than 100 sq. cm. were subsequently increased to 150 and 200 sq. cm.

The epitheliomas of the larynx in females (3 cases cured out of 3 cases treated) received 49 H in 9 days, 54 H in 16 days, and 80 H in 29 days.

In males, we have 19 cured cases, of which 5 were treated during a period of less than 15 days. One patient received 60 H in 8 days; 2 others received 68 and 85 H in 11 days; 2 others 56 and 66 H in 12 days. Eleven patients cured were treated over a period of between 15 and 21 days, with doses averaging between 65 and 71 H. Three patients were cured by treatment extending over a period longer than 21 days: one patient received 71 H in 26 days, another 77 H in 28 days, and a third 75 H in 39 days. A certain number of patients have been treated with 90 and 100 H, but yielded no favorable results.

Up to 1924, the fields were less than 100 sq. cm.; since then they have been increased to 130 sq. cm.

The number of fields or portals of entry has varied between 2 and 4. In cancers of the tonsillar region and lower pharynx, we have usually employed 3 fields on the side of the lesion and one field on the opposite side. Of these 4 fields, the two lateral fields were parallel and crossed by the transverse beams, the three fields on the side of the lesion having overlapping edges. Of the three unilateral fields, the anterior and the posterior were traversed by a sagittal beam, i.e., anteroposterior for one of the fields, and posteroanterior for the other. In this manner, we reduced the useless energy absorbed by the deep tissues, as well as the general accidents which result from it.

In cancer of the larynx, 2 fields have usually been employed, lateral and symmetrical, traversed by transverse beams; an anterior field traversed by an anteroposterior beam has occasionally been utilized.

From the mass of facts which have been cited here, the following conclusions may be drawn:

(*a*) The cutaneous doses which have yielded cures in the three groups of cancer

[2] We have adopted the equivalent of 100 r for 1 H. While this equivalent is convenient it is not absolutely exact. When the field is very small, i.e., when there is a tendency toward the suppression of the secondary rays, 1 H seems to be less than 100 r; if the field reaches large dimensions (300 to 400 sq. cm.) 1 H corresponds to more than 100 r.

have been essentially similar, in spite of the variations in the extent of the lesions, in the surface area and number of fields and in the focal distance. In males, the doses have varied between 65 and 80 H (6,500 to 8,000 r); they have been lower in general for cancer of the larynx and higher for the two other varieties.

(*b*) The increase of dosage above 80 H has not given favorable results, i.e., cures; in the same way, diminution of the doses below 65 H has yielded cures only in women or in cases in which the neck was small.

(*c*) The dose which proved efficacious in the epitheliomas treated seemed approximately the same regardless of the duration of the treatment.

(*d*) The average duration of treatment in the cured males has been 30 to 40 days for the tonsillar region; 24 to 31 days for the lower pharynx and 15 to 21 days for the larynx.

The above conclusions lead to the following considerations:

In proportioning the surface area of the fields to the extent of the lesions and to their depth, we have been led to employ larger surface areas for cancers of the tonsillar region and lower pharynx than for cancers of the larynx. In fact, cancer of the two former locations is deeper and more extensive than laryngeal cancer, and as a rule presents adenopathies by which the epitheliomas of the larynx are rarely accompanied. Thus a patient irradiated through a small field can receive the dose necessary for cure of the neoplasm in a short time, without grave accidents, general or local. A patient irradiated through a large field cannot receive the same dose in as short a time without suffering ill effects. That is why the time of treatment is found considerably increased for the two former groups of cancers (tonsillar region and hypopharynx), whereas it is much shorter for cancer of the larynx. At any rate, it is noteworthy that cancers of the larynx, which are generally the most radioresistant of all the cancers which we have described here, have benefited from the shortest treatments. The conclusion is therefore reached that in epitheliomas whose degree of radiosensitivity is not very different from the varieties of pavement epitheliomas, which we can hope to cure actually, it seems wise to depend upon the dimensions of the neoplasm in deciding upon the duration of the treatment: a very small lesion can be treated in the short time of about 15 days; a lesion of medium size in 20 to 25 days, a very large lesion with large adenopathy in 35 to 40 days; it is altogether impossible to do otherwise in the latter case.

2. *Conduct of treatment. Duration of irradiation. Rapidity of the regression of the neoplasm and of recurrences.*

The continuity of treatment, according to the ideas and experiments of Regaud, has always been respected at all times. When the total duration of treatment has been less than 20 days, the treatment has always been uninterrupted, usually giving two irradiations daily. When the duration of treatment reached 25 days, there were sometimes several days of rest, necessitated by the extreme fatigue of the patient resulting from the use of larger fields. When the duration reached 30 to 40 days, the treatment was either continuous, or more often divided into two or three series of which the first was the most important, the total treatment remaining unified and complete.

In the unsuccessful cases, in which supplementary treatments were attempted, about two to four weeks after the cessation of the first, the results have not been good. Neither has a second complete treatment given good results save in exceptional cases. Among the 55 patients cured locally, 2 patients owe their local cure to a second treatment with roentgen rays given six to seven months after the first.

The average total duration of irradiation has been 25 to 35 hours; the daily dose has varied between 2 H (200 r) per day and 9 H (900 r) per day. The duration of the daily

irradiation has been about 50 minutes in the first case, which gives an hourly intensity of 2.40; it lasted 3 to 4 hours in two daily seances in the second case, which gives an hourly intensity reaching 2.25 to 3; this hourly intensity seems to us not to be excessive.

The neoplastic regression and the disappearance of the glandular masses have been effected after the diverse treatments at irregular intervals. The rapidity of the disappearance of the neoplasm has been the result of numerous factors. Among the most important are: the histological type, the degree of infiltration, the degree of infection and the duration of the treatment.

For the doses indicated, with treatments of 8 to 15 days, the rapidity of the disappearance of the neoplastic lesions has been very marked; after the end of treatment, or at most after 25 days, the neoplasm was no longer appreciable.

In cases in which the epitheliomas definitely disappeared, the result at first seemed excellent, but in these cases we have observed besides sclerodermas and some painful myoscleroses, partial chondro-necroses with elimination of small fragments of cartilage, and also in one case, osteo-radionecrosis of the inferior maxilla which caused death twenty-one months after treatment.[3]

In those cases in which a cure was not obtained, the condition of the patient was aggravated by the treatment given during a short period. Five to six months after treatment one could observe the appearance of multiple edema at the level and in the neighborhood of the irradiated zones. Following this edema, zones of radionecrosis, with very extensive infection appeared in the mucous membrane. Within the sloughing zones the neoplastic development became more rapid and more painful than before the treatment.

Treatment over long periods, from 30 to 35 days, for example, has sometimes led us to fear non-sterilization of the tumor, either during or after the treatment, because the regression of the tumor was sometimes incomplete two months after the beginning of irradiation. In the cured cases, the general condition of the patient was changed before the disappearance of the tumor. In those cases which were not cured, we found neither edema nor zones of radionecrotic destruction; the neoplastic evolution appeared neither more painful nor more rapid than before the treatment; the survival was almost always longer than in the cases which were treated over short periods.

In summary, the lengthening of the duration of treatment has seemed to diminish the number of cures, but has seemed to diminish the rapidity of development of recurrences. On the other hand, the shortening of the duration of treatment has seemed to increase the number of cures, but has seemed to accelerate the rapidity of evolution of recurrences.

3. *Physical conditions of treatment. Physical and biological estimation of doses.*

The tension used at the poles of the roentgen tubes was 130 to 140 kv. in 1920 and 1921, with a filtration of 10, 12 and 14 mm. Al. In 1922, the tension was raised to 175 kv., with 1 mm. Zn, then 1.5 mm. Zn; finally it remained between 175 and 190 kv. for filtrations of 2 mm. Zn plus 3 mm. Al and 1 cm. of wood against the secondary rays from the zinc. In the beginning, the intensity of the current traversing the tubes was 2.5 to 3 ma., until 1921, then from 4 to 5 ma. after 1922. The focal skin distance, first limited to 35 to 40 cm., was increased to 45 to 50 cm. after 1923.

The quantity of roentgen rays has been measured at the skin by means of ionometric apparatus (Solomon, Dauvillier, Bruzeau, Ferroux), or by means of the colorimetric scale of Holzknecht, with disks of platino-cyanide of barium selected and controlled as perfectly as possible.

[3] Among the patients treated in 1927, over short periods, we have seen 2 other cases of osteonecrotic accidents at the level of the inferior maxilla, which caused death two and a half years after the cure. The treatments had been given in 11 and 15 days. We have therefore abandoned these treatments over short periods, except for very small lesions and in particular cases: the endolaryngeal cancers are not treated in less than 15 days; those of the hypopharynx and tonsillar region in not less than 20 days.

The physical conditions and the biological effects were always exactly noted. In this way the measured dose could be evaluated according to the physical constants and in a certain measure controlled by the biological findings.

The precise biological effects are determined under the following physical conditions: focal distance, 50 cm.; field 50 sq. cm.; 4 ma.; 175 kv.; filter, 2 mm. Zn; generators, constant potential of Gaiffe or Veifa Werke apparatus with condensers.

One dose of 45 to 50 H (4,500 to 5,000 r) distributed over ten days in two daily sittings of one hour each or 20 hours, over the same lateral surface of the neck causes at the 26th to the 28th day a cutaneous lesion characterized by a loss of all the epithelial layers with denudation of the dermis; the lesion should be repaired after 15 days, i.e., about the 40th to the 42nd day, without leaving any visible trace; this is the "radioepidermitis" of Regaud and Nogier. If the dose has been greater, the time necessary for the skin recovery is longer; if the dose has been weaker, the time necessary for the recovery of the skin is shorter, as we will show below. The time of evolution of the epidermal lesion can constitute in itself a biological control of the dose.

IV. GOVERNING IDEAS IN THE CONDUCT OF TREATMENT

1. *Production of epithelial radiolesions in the course of treatments given during 1920 to 1926.*

The 42 patients irradiated during the years 1920 to 1926 for epitheliomas of the tonsillar region, hypopharynx and larynx, and actually entirely free of symptoms of cancer have all been treated by the method which we call "epidermicide"; all have presented a "radioepithelitis" of the mucosa and a cutaneous "radioepidermitis." The duration of evolution of the radiolesions was always about thirteen to fifteen days. In the course of these seven years, we have sometimes attempted to reduce the intensity and duration of evolution of the epithelial radiolesions, especially of the radioepithelitis of the mucous membrane. The evolution of this reaction was reduced to ten days and sometimes even to five days; in this manner we spare the patient the pain of the radioepithelitis which is sometimes very marked during movements of deglutition. A recurrence always resulted from this method of treatment.

"Radioepidermitis" and "Radioepithelitis." An observation of the facts leads us to admit that the radiosensitivity of cancer cells of epidermal origin is usually of the same degree as the radiosensitivity of the germinal cells of the epidermis. If one can effect the complete destruction of the germinal cells of the epidermis of the irradiated surface without seriously injuring the dermis, an epidermal cancer of small volume, situated in the same plane in the center of the irradiated surface can also be destroyed. Daily experiences have demonstrated the truth of this elementary principle. Thus, the radioepidermitis that Regaud and Nogier have observed and described in 1913, is characterized by the total destruction of the cells of the germinal layer of the epidermis with denudation of the nearly normal dermis.

The repair of the radioepidermitis occurs from the periphery toward the center, by proliferation of the peripheral epithelial cells, situated along the border of the field, and their development assumes a typical polycyclic appearance, while the derma is slightly modified or not altered at all (Figs. 1 and 2). When the derma has been markedly changed, the repair is effected by proliferation of the peripheral epithelial cells whose development assumes a linear form (Figs. 3 and 4). If not all the squamous epithelial cells in the irradiated field are destroyed, the repair occurs partly from the periphery and partly from the central islands arising from the squamous epithelial cells of the lumina of the sweat glands and of the sebaceous glands (Fig. 5).

In the physical conditions of treatment which we have already indicated, the radioepidermitis appears about the 26th to 28th

FIG. 1. "Radioepidermitis" with derma slightly modified. The proliferation of the peripheral epithelial cells, situated along the border of the field, assumes a typical polycyclic appearance.

day after the beginning of the treatment; it returns to normal in thirteen to fifteen days and terminates at about the 40th to 42nd day, generally leaving no visible sign on the skin surface. The radioepithelitis of the mucosa, or the total destruction of the germinal cells of the epithelium of the mucosa, with denudation of the dermis followed by the formation of plates of false membrane that are more or less thick, appears in the layer of the mucosa at an earlier date, thirteen to fourteen days after the beginning of the irradiation. The duration of its evolution is also about two weeks. At about the 26th to 28th day the radioepithelitis is repaired, leaving not a single trace in the layer of the mucosa. Thus the radioepithelitis completes its evolution at the moment when the radioepidermitis appears, so that the whole of the duration of the irradiation, of the radioepithelitis and of the radioepidermitis will constitute a series of three consecutive periods of about two weeks each, or six weeks (Table VIII, I).

In order to obtain a typical radioepithelitis, it is necessary that the mucosa receive a dose equal to 35 H. If the patient's neck is of small dimensions, one can obtain a radioepithelitis under the conditions indicated above, i.e., when the skin has received 45 to 50 H through a single portal of entry. These cases are exceptional. When the patient's neck is of medium size, in order to obtain the desired reaction in the mucosa one should employ two portals of entry, opposite one another, in order to administer a total cutaneous dose of at least 60 H. This is what we have wished to show in Table VIII when we indicate 45 H through one portal of entry and 15 H through the opposite field.

When the periods of evolution of the two radiolesions overlap (Table VIII, II), i.e.,

FIG. 2 "Radioepidermitis" with derma more modified.

when the radioepithelitis repairs itself only after the 30th, 35th, 40th day, or even later, and when the radioepidermitis appears before the 24th day, even the 20th day, it is because the division of the irradiation has been incorrect, because the doses have been too large, or because the time of the treatment has been too short for the size of the field used.

When the periods of evolution of the two radiolesions are definitely separated, when the radioepithelitis is repaired early, on the 26th, 24th or even 22nd day, and the radioepidermitis does not appear until the 30th or 32nd day (Table VIII, III), it is again because the division of the irradiations has been incorrect; either the doses were too weak or the periods of treatment were too long for the field employed.

Under these circumstances, the radioepithelitis and radioepidermitis repair in five to ten days and there is great possibility that a cancericidal effect, at the site of the primary lesion and of the lymphatic glands, has not been produced.

FIG. 3. "Radioepidermitis" with derma greatly modified.

FIG. 4. The repair is very slow. The proliferation of the peripheral cells assumes a linear form.

The duration of the evolution of the radiolesions thus constitutes a sufficiently exact control of the phenomena obtained at the end of the irradiations and consequently a control of the correct division of a treatment. But the conditions of treatment described above are appropriate only for a small lesion and for a small field, which renders a short treatment possible; it is a scheme of minimum duration of treatment. It can be considered as a typical treatment of a very small non-infiltrating epithelioma of the larynx that is not adherent to the cartilage.

The conditions are necessarily different when the lesions are more extensive, necessitating the use of larger fields and consequently longer periods of treatment.

These therapeutic indications can only be very incomplete because, besides the

small variations in the time of appearance of the radiolesions of the mucosa in general, and in the duration of their evolution in different individuals irradiated under identical conditions, one can observe in the same individual on the surface of different segments of the mucosa, the radioepithelitis occurring at different times.

The different times of appearance of the radioepithelitis are caused by the notable differences in the cellular types which cover

FIG. 5. The repair assumes on the anterior border a polycyclic appearance, on the posterior border a linear form, and takes place partly from the periphery and partly from the central islands.

the segments considered. They can be produced by variations in the daily division of doses, duration of irradiation and total duration of the treatment.

In general, the most radiosensitive of all the mucous membranes, that in which the radioepithelitis appears first, is the mucosa at the union of the pillars and the uvula. Under the conditions stated, it becomes covered by false membranes on the 13th day, one day before the posterior wall of the hypopharynx; the vallecular regions, the origin of the pharyngo-laryngeal furrows and the floor of the mouth have their reaction somewhat later. The mucous membranes which cover the cheeks, the horizontal and vertical branches of the inferior maxilla, become covered by false membranes about the 16th day, and their radioepithelitis demands slightly higher doses. The laryngeal surface of the epiglottis, the laryngeal part of the interarytenoid space, and the base of the tongue, are not covered by false membranes until about the 18th day. The vocal cords, the dorsal and anterior surfaces of the tongue do not become covered with false membranes until the 20th day; sometimes the 22nd day, and in response to higher and higher doses.

The differences in the dates of appearance of the radioepithelitis for the different segments of irradiated mucous membranes throw some light on the difference in radiosensitivity of different segments of mucosa; they correspond roughly to the same difference in the radiosensitivity of epitheliomas developed in the areas of these diverse segments. These are the indications that are sometimes of importance in the choice of duration of the treatments.

2. *Doses and cancericidal effects.* To sum up, if the field is small and if the distribution of irradiation is accomplished in the maximum period of fifteen days, we consider that the doses capable of provoking the destruction of epithelial cells correspond, for the skin, to 45 H (about 4,500 r); for the mucous membranes to 35 H (about 3,500 r). The doses necessary for the destruction of epitheliomas whose radiosensitivity is similar to that of cutaneous epithelium should reach 45 H (about 4,500 r). The dose necessary for the destruction of epitheliomas whose sensitivity is analogous to the epithelial cells of the mucous membranes is about 35 H (3,500 r). These doses which should necessarily be modified according to intervening infection, deep in-

filtration, or adherence to the cartilages, have permitted us to cure some cancers more easily because of their greater radiosensitivity. In order to attain these doses in the area of the lesion to be destroyed, we have been obliged to utilize, for the combined portals of entry, a total dose nearly double the preceding one.

We have seen that in the treatment of pavement epitheliomas there is no relation, up to a certain limit, between the doses received and the frequency of cures, regardless of the degree of radiosensitivity. Our patients have been cured with doses between 7,000 and 8,000 r, or 70 to 80 H. When the doses have reached 90, 100, 120 and 150 H, there was no cure; on the contrary, aggravation of the patient's condition and increased rapidity of recurrence have been the rule.

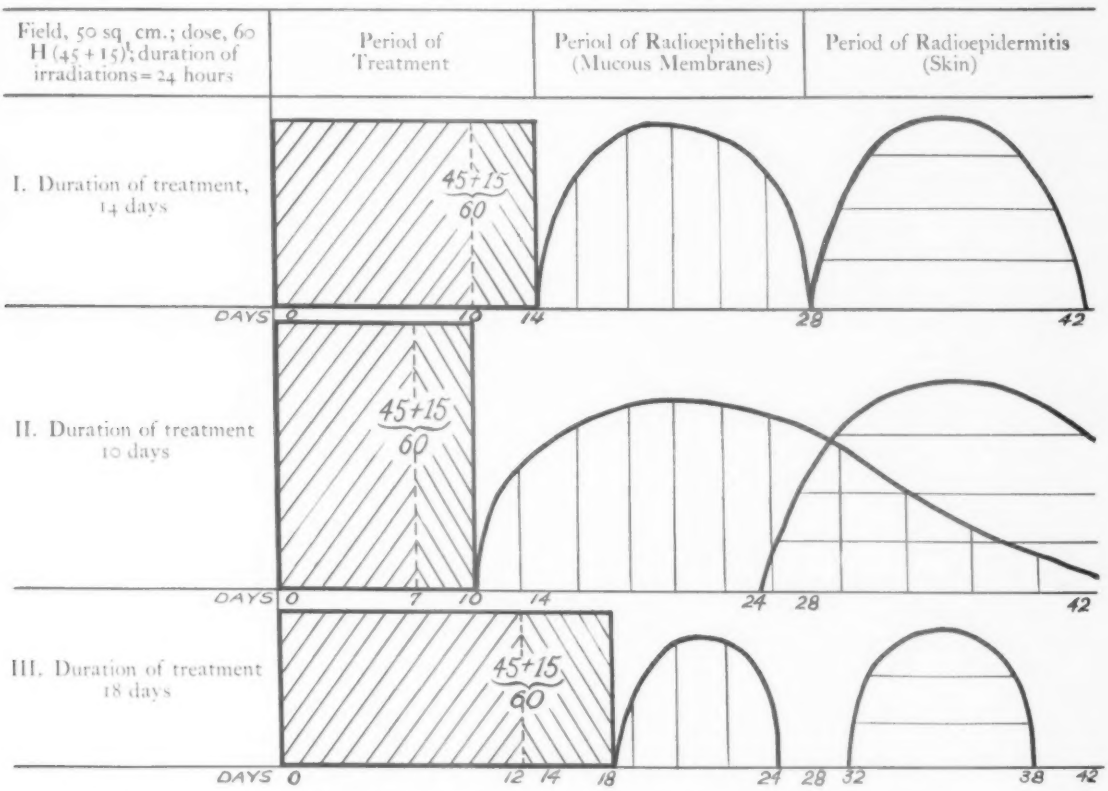
Under the conditions in which our treatments were conducted, the cancericidal effects did not increase proportionately with the doses, beyond a certain value.

Neither do the cancericidal effects increase proportionately with the time of treatment—quite the contrary. The real or apparent loss of radiosensitivity (immunization) of the cells of squamous epithelioma is often appreciable about the 30th day after the beginning of the treatment. In the same way, the epithelial radiolesions of the skin and mucous membranes are more difficult to provoke (even when

TABLE VIII

FIGURES ILLUSTRATING THE EVOLUTION OF MUCOUS MEMBRANE AND CUTANEOUS LESIONS OF THE NORMAL EPITHELIUM IN ROENTGEN THERAPY OF SQUAMOUS EPITHELIOMAS OF THE HYPOPHARYNX AND LARYNX.

The Whole is Composed of Three Equal Periods of Two Weeks Each or Six Weeks.


Field, 50 sq. cm.; dose, 60 H (45+15)[1]; duration of irradiations = 24 hours
Period of Treatment
Period of Radioepithelitis (Mucous Membranes)
Period of Radioepidermitis (Skin)
I. Duration of treatment, 14 days
45+15
60
DAYS 0 10 14 28 42
II. Duration of treatment 10 days
45+15
60
DAYS 0 7 10 14 24 28 42
III. Duration of treatment 18 days
45+15
60
DAYS 0 12 14 18 24 28 32 38 42

[1] 45 H is given to one side of the neck; 15 H to the other side.

the doses are slightly increased) the longer the treatments have lasted.

V. COMPLICATIONS AND ACCIDENTS

The complications and accidents observed during the course of our treatments have been due, on the one hand, to connective tissue vascular lesions and, on the other hand, to toxic phenomena in which the chemical transformations of the connective tissue probably play a part.

The caustic or semi-caustic methods have often yielded cures of small superficial epitheliomas or of those situated in a particularly tolerant zone. The connective-vascular tissue was greatly modified at the same time that the epithelioma was destroyed. When one deals with cancers located in the larynx, mouth and pharynx, a more selective method (cytocaustic electivity of Regaud) must be employed in order to protect the tissues surrounding the neoplasm. With roentgen rays we have not obtained cures of epitheliomas in these locations in treatments of less than eight days.

When the epithelioma is further developed and more deeply situated in the cervical region, and when more extensive fields are employed, the necessity of protecting the connective tissues becomes more and more important, and this fact necessitates a prolongation of the time of the treatment, for the post-roentgen complications always take on a graver aspect as the total duration of treatment is shorter and the number of hours of irradiation is less.

The complications which we have observed have been local or general, immediate or late.

1. *Immediate local complications.* The first of all the complications is characterized by the appearance of a precocious edema. The precocious edemas are glandular, appearing in the region of the parotid, submaxillary and sublingual glands; they are also subcutaneous. They often appear at the beginning of the irradiation, disappearing after about twenty hours and re-appearing during the second irradiation; sometimes they are slight, sometimes they become chronic during the course of treatment, leaving characteristic changes in the appearance of the chin and face.

The precocious edemas also occur in the deeper tissues and are to be seen in the mucous membranes at the same time that they are visible in the neoplasm itself. In the cancers of the larynx and hypopharynx, if edema appears before the neoplasm has regressed, it provokes dyspneic accidents which necessitate tracheotomy.

Parallel with the edemas, there frequently appear intense and early cutaneous erythemas accompanied by enanthemas of the mucous membranes.

The importance of these edemas, erythemas, enanthemas and their extent, the intensity of the pain which accompanies them and their tendency to chronicity, vary with the size of the fields, the hourly and daily intensities, the daily and total doses, and the previous state of the capillaries. When they are very intense and early, the edemas and erythemas constitute proof of disturbances in the subcutaneous and submucous blood capillaries. They seem to modify unfavorably the radiosensitivity of the epitheliomas and their adenopathies; they are also an important factor in the appearance of late complications.

Sometimes the treatments have caused more or less important early hemorrhages following the sudden melting of the neoplastic masses, due to the local congestion secondary to the irradiation. They have also occasioned the development of inflamed glands with elevation of temperature and acute perichondritis; not only have these accidents been serious in themselves, but they have nearly always necessitated the abandonment of treatment, thus leading to failure.

There exists a series of early local complications, difficult to avoid, but much less grave. They are: dryness of the mucous membranes of the mouth and pharynx, with thickening of the saliva; perversion or complete loss of taste due to modification

or diminution of glandular secretions; dysphagia, which precedes the radioepithelitis of the mucous membranes; the radioepithelitis of the mucous membranes themselves, a complication still inevitable because when we have wished to reduce or suppress it, we have been unable to effect a cure; finally the cutaneous radioepidermitis which as far as we can see, constitutes a complication only when its restoration is late.

From time to time during the course of treatment, we have encountered myoclonic crises in the muscles of the neck, arms and trunk, and paresis of the arms and legs which have never lasted more than one or two months.

2. *Late local complications.* These have been the result of the tendency to chronicity of the complications indicated above: the persistence of the dryness of the mucous membranes and of the perversion of taste lasting sometimes as long as one or two years; the chronic edemas constantly becoming harder and thicker and developing into a scleroderma; in certain cases we found cutaneous atrophy with discoloration of the teguments, adherence of the skin to the deep osseous or cartilaginous structures, and a mottled appearance of the skin with telangiectasis. In other cases there appeared a chronic myositis sometimes composed of simply a muscular retraction; at other times by a muscular inflammation simulating a diffuse glandular recurrence. The sensation of painful muscular contraction in the entire irradiated region has been noted five to six years after treatment without a single muscle appearing to be especially diseased.

All these symptoms can be the sign of graver chronic lesions, such as radiodermatitis with ulceration of the dermis and secondary infection, and osteo-radionecrosis or chondro-radionecrosis which can cause death by infection or hemorrhage. The late rupture of vascular walls in the neighborhood of a radionecrotic zone in the soft parts has been observed several times. Furthermore the vessels have often been modified by the irradiation even in the absence of radionecrosis in their zones or neighborhood; particularly the formation of aneurysmal dilatation in the region of the carotids two years after treatment has been observed in 4 patients.

In certain cases of intense irradiation with cure, we have observed late neuritis with muscular atrophy and more or less complete paralysis of the subspinous muscle, deltoid, and trapezius; they appear to be the result of compression of the nerve trunks of the cervico-brachial plexus by the deep sclerotic connective tissue; sometimes it was only a simple local neuritis without muscular atrophy of appreciable weakness.

We have also observed following very extensive intense irradiation for epitheliomas of the tonsillar region, deafness due to sclerosis of the tympanic membrane and ossicles appearing three to six months after treatment, and cataract formation developing two years after irradiation when ocular protection has been impossible.

Most of these immediate or late local accidents are avoidable:

(*a*) By watching and reducing the intensity of the treatments, i.e., by lengthening as much as possible the total duration of the treatment when the neoplastic lesions are larger and the fields of exposure cover a greater surface area. If for fields of 80 sq. cm. the treatment is extended over 20 days, the same skin doses should be extended over 25 to 30 days for fields of 150 sq. cm. A dose of 6 H (about 600 r) daily should usually not be exceeded. A dose of 50 H which can be given in 10 days over a single field of 50 sq. cm., should be reduced to 35 or 40 H and given in 16 to 17 days for a single field of 150 sq. cm.

(*b*) By taking prophylactic measures against the secondary causes of accidents. In order to fight against the possibility of osteo-radionecrosis of the inferior maxilla which we have observed one, two and even five years after treatment of epitheliomas of the tonsillar region, we at one time made a practice of resecting the angle of the inferior maxilla before treatment. This meth-

od, however, did not yield favorable results.

The extraction of all teeth on the side of the lesion, meticulous cleaning of the teeth on the opposite side, with the extraction of roots and teeth in bad condition, are essential and constitute the minimum of precaution. We thus avoid infection, the essential cause of osteonecrosis, and we avoid the possibility of extraction after treatment at an inopportune time, which has nearly always been the cause of necrosis of the inferior maxilla.

In order to avoid osteo- or chondro-necrosis following roentgen therapy of epithelioma of the larynx or hypopharynx we have made a practice of resecting the thyroid and cricoid cartilage on the side of the lesion, especially when they were frankly ossified. This operation which is advantageous becomes indispensable when the cancer has invaded the cartilages, is deeply infected and only slightly radiosensitive. Most of the bony or cartilaginous necroses of the larynx are due, in fact, much more to the invasion of the cartilage by the neoplasm than to the effect of irradiation.

The accidents which we have just described are much less likely to occur when we take these precautions and when the treatments are divided over a longer time, using larger fields. But in these cases of very extensive fields, other varieties of accidents appear: these are the complications or accidents of a general nature; they can be early or late

3. *Early and late general complications.* Those that appear first are the disturbances of the digestive apparatus, such as nausea and vomiting. They are very frequent complications but they are often of little importance. They occur more frequently in women than in men. They indicate the limit of individual tolerance. It is only necessary to lower slightly the daily doses and to reduce the size of the fields to cause the symptoms to disappear without discontinuing the treatment.

The hepatic complications are more serious. They are characterized by a passing subicterus with elevation of temperature, but we have sometimes found, besides a marked and persistent icterus, an enlargement of the liver accompanied by a sensation of local tension. In 2 cases where the treatment was intense with rather large fields, the jaundice ended in death, occurring twenty-five days after the beginning of the treatment in one of the patients and three months in the other.

The slight hepatic disturbances have often been accompanied by cutaneous manifestations of a toxic nature which appear sometimes five to six days, one month, and more rarely, two to three months after the beginning of treatment. The most frequent have been: erythema nodosum, especially located in the legs; urticaria, in the thoracic, abdominal and brachial regions, and palmar or plantar eczematoid eruptions. The duration of these cutaneous manifestations was at the most one to one and a half months. Diverse inflammations or articular congestions of the same nature have been observed at different times. These generally less serious complications have not influenced the progress of treatment.

It is different with the cardiac complications. They often constitute an obstacle to the completion of the outlined irradiations. They are characterized, after two or three weeks, by a marked asthenia, a lowering of the maximal arterial tension with a tendency to annul the pulse pressure. These symptoms are sometimes accompanied by signs of acute or chronic myocarditis and as we have observed in 2 cases, can cause death. They are always marked when we utilize large fields, even if the daily doses are weak; they are rare if we use small fields, even if the daily doses are high. They can be attributed to the association of toxic phenomena (liberation of chemical products especially from the connective tissue). In the cardiopaths, roentgen therapy of cancer is always very difficult and very imperfect. The results are usually unsatisfactory on account of the impossibility of regular treatment even if the size of the fields is reduced. In these patients bron-

chopneumonia is a frequent complication and sometimes occurs during the radioepithelitis, when the larynx and hypopharynx are filled with false membranes.

The loss of weight is often considerable during the course of treatment. When the doses and the fields are not proportioned to the tolerance of the patient, the loss of weight may reach 15 to 20 kilos in one month. Thus, in a patient who has been weakened and emaciated previously by the development of the epithelioma, this additional loss of weight as a result of roentgen therapy still further reduces the chances of success.

In the cervical regions, a field of 150 sq. cm., with daily doses of 400 to 500 r, causes a rapid loss of weight. If cervical fields, not exceeding 50 to 60 sq. cm. are utilized, the loss of weight is generally negligible even for the high doses. In the tuberculous the loss of weight is very rapid and often compels a postponement of the treatment.

After the cancer has disappeared, the patient rapidly regains the lost weight. Some of these, however, regain only a small part of their weight; they are the patients in whom the treatment has been poorly adapted to their physiologic state and whose organism has been greatly modified. They remain extremely delicate and the slightest intercurrent affection takes on a grave aspect. Three of our patients in whom the treatment was too intense have died.

We have encountered no changes in the blood picture which could be considered as a complication.*

* For discussion see page 343.

DEVELOPMENT OF TECHNIQUE AND RESULTS OF TREATMENT OF TUMORS OF THE ORAL AND NASAL CAVITIES*

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FIRST of all, I wish to express my deep and sincere gratitude to the American Roentgen Ray Society for the great honor conferred upon Swedish radiology and particularly upon the Radiumhemmet, by inviting me to read a paper before this illustrious gathering.

In Sweden, ever since the year 1909, when the Radiumhemmet was founded, radiotherapy has been centralized in a few radiotherapeutic clinics. From the very beginning the pioneers of the new science, Dr. Gösta Forssell above all, realized the great importance to medicine of the new physical aids, roentgen rays and radium, and the necessity for developing them into a new and independent science. The course of events has proved the correctness of this idea.

After the labor of the first few years in developing, chiefly empirically, a technique for treatment, the need of a physicist for standardization of the dosage and for scientific research work in the field of radiophysics became more and more keenly felt. Thus, there was established the Radiumhemmet's physical laboratory, where at present five physicists are at work.

Radiotherapy has likewise given rise to a new branch of histopathology, namely, radiohistology, embracing the study of the changes brought about by irradiation in normal and tumor tissue, the classification of tumors, etc., which called for pathologists especially interested in this branch. As a consequence, the histopathological department of the Radiumhemmet, including a section for research work, particularly tissue culture and concomitant problems, was established.

The Radiumhemmet has gradually been organized and built up into an institution for the study and treatment of malignant diseases. It consists at present of: (1) a clinical department with accommodations for 56 in-patients; (2) an out-patient department; (3) an operating room chiefly for electro-endothermy and minor surgical procedures; (4) a radium therapy department; (5) a roentgen therapy department with 6 apparatus; (6) a record, follow-up and statistical department and library; (7) a social service department; (8) a physical laboratory, and (9) a histopathological laboratory and research department. Through the work of the follow-up department, we are able to keep track of all our patients. We know, for instance, the results of the treatment of the 2,000 patients suffering from uterine carcinoma treated from 1914 to 1930 inclusive.

At the present time, Radiumhemmet has at its disposal 5.026 gm. of radium element in the form of sulphate of radium distributed among 114 tubes and needles, 35 flat applicators and 70 tubes for teleradium treatment.

There are now in Sweden three radiotherapeutic centers for the treatment of malignant tumors, namely, the Radiumhemmet in Stockholm, for a population of approximately 3½ millions (northern and central Sweden), the radiologic clinics at Lund, for a population of 1,350,000 (southern Sweden), and at Göteborg for a population of likewise 1,350,000 (western Sweden). The clinics at Lund and Göteborg are organized as radiotherapeutic clinics along the lines of the Radiumhemmet.

The superiority of the radiologic clinics

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is due partly to the advantages resulting from the possession of large quantities of radium and other therapeutic agents, and to their better organization, partly to the constant close cooperation between the surgically trained radiologist, the physicist and the pathologist, who are jointly endeavoring to reach the same goal, i.e., the development and improvement of the therapeutic methods in treating malignant tumors for the welfare of the patients.

Experience has shown that really satisfactory work for combatting malignant disease can be carried out only at institutions organized upon this principle, with scientists who are devoting their lives and interest entirely to this work. An organization which tolerates the splitting up of the quantities of radium and other therapeutic means among minor institutions, and their handling by physicians whose interests are directed towards other fields, e.g., pure surgery or pure gynecology, without the assistance of a physicist and a pathologist, has been found to give unsatisfactory results in the treatment of malignant diseases.

One of the most difficult problems in the development of radiotherapy has been, and still is, the treatment of tumors in the upper alimentary tract and in the air passages. The causes of this are: (1) the difficulty of making an early diagnosis; (2) the high degree of malignancy; (3) early disintegration and septic secondary infection; (4) early invasion of bone and cartilage; (5) early effect on the patient's condition; (6) the failure of surgical intervention; (7) low degree of radiosensitivity of the tumor cells, and (8) high degree of radiosensitivity of the surrounding tissues.

Tumors in the oral and nasal cavities often display a very rapid local infiltration and an early and frequent explosive spread to the regional lymphatic glands. Broders has emphasized these clinical facts in his grading of the potential malignancy of tumors which he based on the differentiation of tumor cells with reference to the results of surgical treatment and not of radiotherapy (Table 1).

Of carcinomas of the tongue most cases, 47 and 46 per cent respectively, belong to Grade II and III and of carcinomas of the tonsil, most cases, 35 and 58 per cent respectively, belong to Grade III and IV. Of these localizations only about 40 per cent are operable when the diagnosis is first made, and the results of surgical intervention show about 20 per cent of primary healing with the exception of the tonsillar tumors where, practically speaking, no cure has been obtained with surgery alone.

TABLE I

BRODERS' GRADING OF POTENTIAL MALIGNANCY

	Carcinoma of			
	Tongue	Gums; Lips	Tonsils	Pharynx
	per cent	per cent	per cent	per cent
Grade I	1.28	7.60	—	—
Grade II	47.43	54.38	5.88	47.05
Grade III	46.15	34.50	35.29	35.29
Grade IV	5.12	3.50	58.82	17.64
Good Results of Surgical Treatment	20.44	28.73	0	16.66

The majority of malignant tumors in the oral and nasal cavities belong to the adult type of epidermoid carcinoma, which show a very low degree of radiosensitivity. Martin and Quimby have thus shown that it requires about 7–10 S. E. D. at all points within the tumor-bearing area to produce complete retrogression of these adult carcinomas. The rarer undifferentiated types of tumors require about half this intensity.

The problem of dosage, therefore, stands out as a central one in dealing with these tumors.

Experience very soon taught us that it is impossible to apply the necessary dose to a tumor in the oral cavity merely by external treatment without causing local necrosis which impairs the result and without deleteriously affecting the patient's general condition. As a rule, there should be a combination of the different forms of ap-

plication of radium or roentgen rays with surgery, carefully taking into consideration the histological structure of the tumor and the physical dosage. The treatment of a patient suffering from a malignant tumor has to be planned and carried out in the closest cooperation between clinician, radiologist, surgeon, physicist and pathologist.

Fig. 1. Lysholm's teleradium therapy apparatus (1922).

One of the first principles adopted by Forssell (1914) in the planning and elaboration of the methods of treatment was, on the one hand, to weaken the tumor's capacity for growth so much that the natural healing powers of the patient's organism could then successfully combat the disease; on the other hand, to avoid causing such damage either to the healthy tissues surrounding the tumor or to impair the general power of resistance of the body, as might make the latter incapable of reacting against the weakened tumor.

We have tried on the basis of this principle by means of radiotherapy to diminish the size of the tumor as much as possible and to delineate the same against the surrounding tissues. In those cases where the tumor does not disappear by the radiological treatment we subsequently remove, to an increasing degree, the remaining resistant tumor remnants with a minor surgical intervention, mostly by endothermy.

The methods of treatment of malignant tumors of the oral and nasal cavities, employed at the Radiumhemmet are, therefore, as a rule combined: (1) preoperative radiological treatment, and (2) ensuing operation. It must, however, be borne in mind that the radiological treatment of malignant tumors is by no means standardized, but the very greatest consideration has to be taken of the different individual variations, both in respect to the site, spread, radiosensitivity, etc., of the tumor and in regard to the patient's general condition, his age, manner of reaction, etc. No two tumors are alike, and the key to successful radiotherapeutic treatment is a careful study of the biological characteristics of the tumors and their reaction to the treatment. It is only in the hands of the experienced radiologist that a favorable result of healing can be attained.

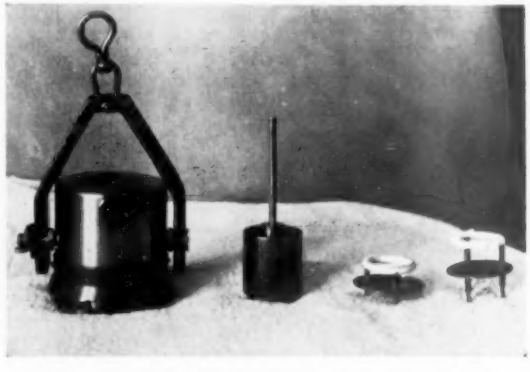

Fig. 2. Lysholm's teleradium therapy apparatus (1922), showing the protective lead cylinder, the radium container and the filter for the secondary rays.

The therapeutic means at present employed at the Radiumhemmet for malignant tumors in the oral and nasal cavities are: for the primary tumor, (1) teleradium therapy; (2) local surface contact applica-

tion; (3) implantation of radium needles, and (4) endothermy; for the glandular regions, teleradium therapy, sometimes in combination with conservative surgery. Roentgen treatment is nowadays resorted to as a rule only in the radiosensitive forms of tumors, such as lympho-epithelioma and sarcoma, since radium according to our experience is incontestibly superior to roentgen rays in the treatment of adult epidermoid carcinoma.

We began to make use of the teleradium treatment in the year 1922, in the form of radium packs as used at the Memorial Hospital in New York. In the same year Lysholm designed our first teleradium

Fig. 3.

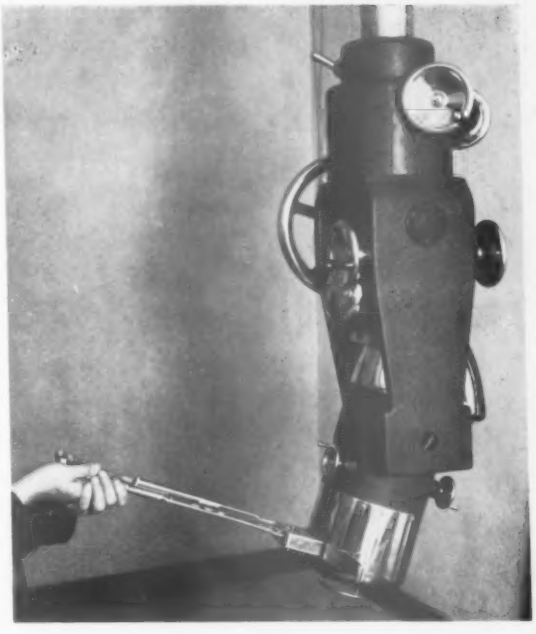

Fig. 4.

therapy apparatus, which gave protection to the surrounding tissues, as the radium was encased in a lead cylinder with a wall 2 cm. thick. The secondary radiation was eliminated as much as possible by a brass filter applied half the treatment distance according to Sievert (Figs. 1 and 2).

In the year 1929 the Radiumhemmet received 3 gm. of radium, chiefly for teleradium treatment. With the increased quantities of radium and the improved facilities for treating a greater number of patients the primary therapeutic result was greatly improved. Our present teleradium apparatus was designed by Sievert (Figs. 3 to 6). The different possibilities of adjustment will be distinctly seen from the figures. In case a large area is to be treated the thicker end of the movable cylinder is used, but for smaller fields which are difficult of access, the smaller curved end of the cylinder (Fig. 3.) is resorted to. The radium-bearing capsule contains 3 gm. of radium divided into 60 tubes of 50 mg. radium element each, and can be moved from one end to the other with a single manipulation by means of a specially designed forceps (Figs.

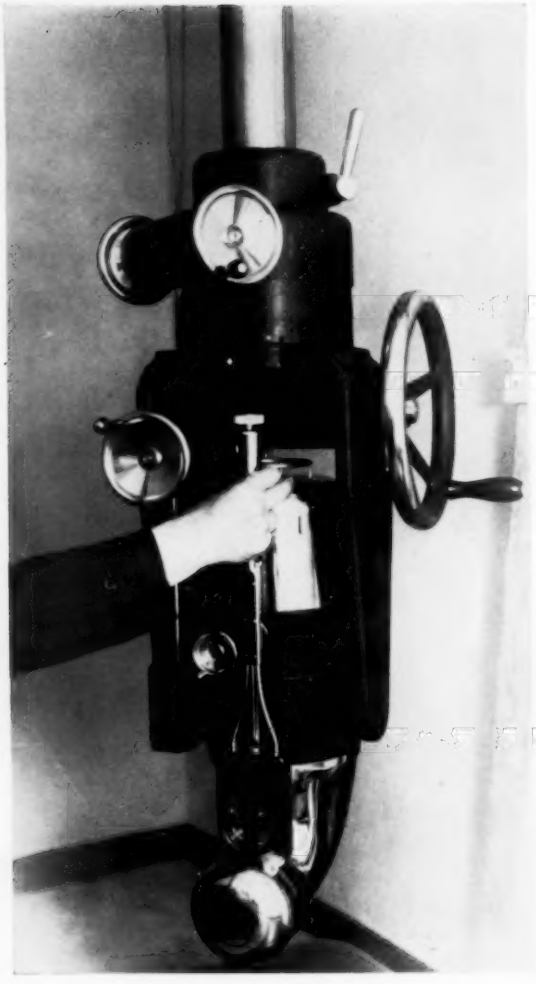

Fig. 5.

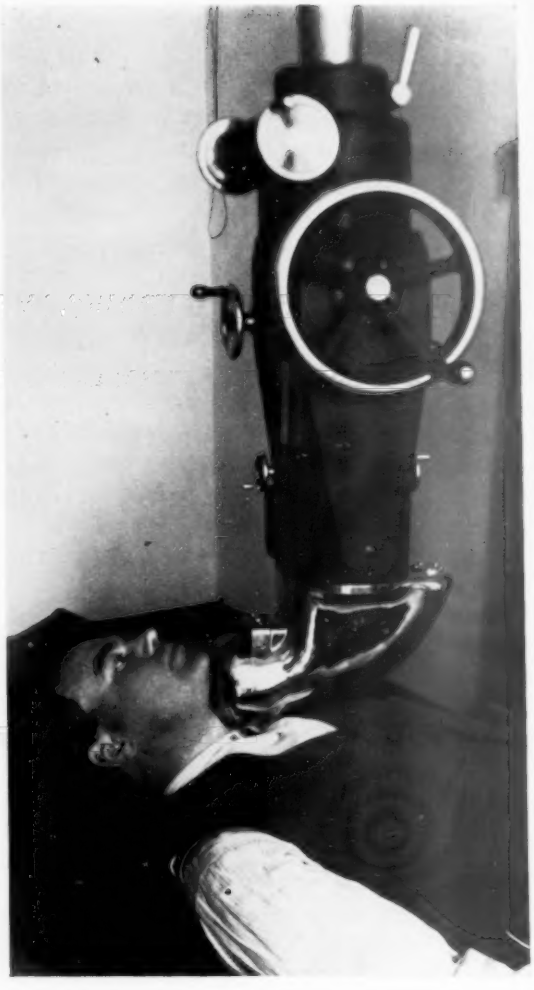

Fig. 6.

4 and 5). The application is easy and compression is possible, as will be seen from Figure 6.

The filter is equivalent to 5 mm. of lead, the distance is 6 cm. and the lead protection against the surrounding areas varies between 2.5 and 6 cm.

In local surface contact application into the oral and nasal cavities the radium tubes are applied with dental compound. The treatment filter is equivalent to 1–3 mm. lead. This technique of application has now been largely superseded by implantation. In interstitial implantation, radium needles containing 5–10 mg. radium element and provided with a gold platinum filter equivalent to 1 mm. lead, are inserted into and around the tumor area.

In all of our treatments of tumors in the oral and nasal cavities we thus employ consistently only the very short wave-length gamma radiation, filtered through at least 1–6 mm. lead. We are fully convinced of the superiority of this hard radiation over any softer radiation.

Endothermy is performed by the bipolar method with coagulation of the tumor area and its surroundings. The coagulated portions are then left to slough off spontaneously. The heat, endogenously generated and the intense reactive exudative inflammation in the surrounding tissues may pos-

sibly be of importance in overcoming existing tumor remnants outside the necrotic area (Westermark).

Carcinoma of the tongue was treated chiefly with external roentgen and surface contact application of radium tubes against the surface of the tumor, during the period from 1916–1922. In those days the available quantity of radium did not permit of any teleradium treatment or interstitial implantation.

In 1922 we began with teleradium therapy at a distance of 5–6 cm. the dose being given in the course of about three weeks. But during the last three years the total dose has been increased to 50–150 gm-hr. It causes on the skin over the diseased side an epidermitis (Regaud-Nogier) and on the tumor area an epithelitis (Coutard). After these reactions have passed off, which takes about four weeks, endothermy is applied to the tumor remnant in the form of bipolar coagulation. Upon completion of this coagulation, and while the patient is under the influence of the anesthetic, radium needles are implanted at the border between the coagulated portion and the healthy tissue. The time for the treatment is only three to four hours and the coagulated portions are left to slough off spontaneously. In the case of larger infiltrating tumors a ligature of the external carotid is made prior to coagulation, so as to obviate bleeding. During the first period, 1916–1921 inclusive, we treated 54 cases and 17 of them, or 32 per cent, were living for five years or more. During the period 1922–1926 inclusive, we treated with the increased dose of teleradium altogether 50 cases and of these 16, or 32 per cent, have been living free from symptoms for five years or more (Table II).

The percentage of healing is the same in both periods but a review of the cases shows that the material was poorer during the later period in that more advanced cases have been brought under treatment as is shown by Table III.

TABLE II

FINAL RESULTS IN CARCINOMA OF THE ORAL CAVITY

	1916–1921 incl.		1922–1926 incl.		1916–1926 incl.	
	Number of Cases	Free from Signs and Symptoms 5 Years or More	Number of Cases	Free from Signs and Symptoms 5 Years or More	Number of Cases	Free from Signs and Symptoms 5 Years or More
Carcinoma linguae	54	17 (32%)	50	16 (32%)	104	33 (32%)
Carcinoma sublingualis	11	5 (46%)	21	6 (29%)	32	11 (34%)
Carcinoma mandibulae	27	3 (11%)	34	8 (24%)	61	11 (18%)
Carcinoma buccae	43	9 (21%)	38	12 (32%)	81	21 (26%)
	135	34 (25%)	143	42 (29%)	278	76 (27%)

TABLE III

CARCINOMA OF THE TONGUE 1916–1921 AND 1922–1926 INCLUSIVE

Results depending upon spread of tumor

	1916–1921		1922–1926	
	Number of Cases	Free from Signs and Symptoms 5 Years or More	Number of Cases	Free from Signs and Symptoms 5 Years or More
Group I*	33 (61%)	16 (49%)	27 (54%)	16 (59%)
Groups II and III	21 (39%)	1 (5%)	23 (46%)	0
Total	54	17 (32%)	50	16 (32%)

* Group I cases without metastases.

Groups II and III cases with mostly inoperable metastases.

In judging the results of healing we have to remember that the material does not consist of selected cases. Many patients when first seen have extensive tumors with inoperable metastases, and are in such a poor state of health that any attempts at curative treatment would only injure the patient. In these cases we have to confine ourselves to giving palliative treatment, as these tumors are never suitable for coagulation. By employing, during recent years, more and more our technique of teleradium therapy, endothermy and implantation of radium needles, we have reached, for example, in the year 1928 three year healing results, and in the year 1929 two year healing results in 42 per cent of the cases treated.

In the other tumors of the oral cavities the development of our technique has been carried on along the same principles, and the results obtained from the treatment have been gradually improved, with the more intensive use of teleradium treatment and the combined coagulation and interstitial implantation of radium needles.

Carcinoma of the sublingual region is now treated with the same technique as carcinoma of the tongue.

Of 11 cases of carcinoma of the sublingual region treated during the period from 1916–1922 inclusive, 5 became free from symptoms for five years or more, i.e., 46 per cent, whereas during the ensuing period from 1922–1926 inclusive, only 29 per cent were free from symptoms (see Table II). The cause for this drop in the percentage of cures is due to the fact that during the later period the material was much worse, in that no fewer than 53 per cent of the cases on admission had widespread metastases (Table IV).

In the cases of mandibular carcinoma we begin with teleradium treatment covering the primary lesion and the glandular region, for a total of 50 gm-hr., and follow this with endothermy. During the latter period, 1922–1926 inclusive, we obtained an improved result, in that in 24 per cent, a five year freedom from symptoms was attained, while the freedom from symptoms during the former period remained at 11 per cent.

In both these locations the radiation treatment is difficult because necroses may easily make their appearance in the underlying bones, and these impair the prognosis considerably. Endothermy of minor tumor remnants constitutes here an improvement of the technique. Those sequestrations that occur after endothermy do not cause any severe pain and are made to disappear in three to six months, after which the wound heals rapidly leaving a soft scar.

TABLE IV

CARCINOMA SUBLINGUALIS 1916–1921 AND 1922–1926 INCLUSIVE

Results depending upon spread of tumor

	1916–1921		1922–1926	
	Number of Cases	Free from Signs and Symptoms 5 Years or More	Number of Cases	Free from Signs and Symptoms 5 Years or More
Group I*	9 (82%)	5 (56%)	10 (47%)	6 (60%)
Groups II and III	2 (18%)	0 (0%)	11 (53%)	0 (0%)
Total	11	5 (46%)	21	6 (24%)

* Group I without metastases.
Group II with mostly inoperable metastases.

Carcinomas in the cheek are, from a therapeutic-technical point of view, a very difficult problem because they are located in the thin cheek with very poor capacity of resorption and reaction, and close to the radiosenstive alveolar processes, which are frequently infiltrated by tumor growth. Before 1921 these tumors were being treated with external roentgen radiation and surface contact application of radium tubes. After 1921 the external treatment with teleradium was used more and more. After the tumor ulceration has become clean, smaller and better localized, electro-endothermy is employed in the form of bipolar coagulation between two flat electrodes.

In the case of infiltration of the alveolar process even the latter is coagulated to a

sufficient extent. The results have been greatly improved during the latter period, in that 12 out of 38, or 32 per cent, have become free from symptoms for five years or more, whereas during the former period only 21 per cent became free from symptoms for the same period.

The results from the improvement in technique during the years 1922 to 1926 have thus become manifest in a higher percentage of healing, particularly in view of the fact that during the latter period more advanced cases have been submitted for treatment.

As a final result of the treatment during the eleven year period, 1916–1926 inclusive, there remains a cure for 5–11 years of 75 out of 278 patients, suffering from lingual, sublingual, mandibular and buccal carcinoma, or 27 per cent.

Tonsillar carcinomas are among those tumors which have given poor results with all methods of treatment until quite recent years. Surgical treatment is hardly able to show a single case of healing. With endothermy some authors have succeeded in healing well-confined tonsillar tumors, but no very extensive statistics are available.

Prior to the year 1924, tonsillar carcinomas were treated at the Radiumhemmet with external roentgen radiation with 0.5 mm. Cu filter at a distance of 30 to 40 cm. followed by surface contact applications of radium tubes. With this therapeutic technique primary healing was obtained in 25 per cent of 28 cases, but this primary healing did not remain permanent. All the patients died within three years (Table v). Since 1924 we have been using external treatment with teleradium (5 mm. lead equivalent filter, 6 cm. distance, total dose 100–150 gm-hr.). After the tumor had diminished local treatment was resorted to, either with surface contact application, implantation of radium needles, or endothermy of minor tumor remnants. Altogether 18 cases of carcinoma and lympho-epithelioma were treated during the period 1924 to 1927, inclusive. Of these 18 cases 7, or 39 per cent, have been living for more than three years (Table VI).

TABLE V

PRIMARY HEALING AND THE HEALING AFTER ONE, TWO AND THREE YEARS IN 28 CASES OF CARCINOMA, TREATED 1919–1924 INCLUSIVE BY THE OLD TECHNIQUE

Group*	Primary Healing	Free from Signs and Symptoms 1 Year or More	Free from Signs and Symptoms 2 Years or More	Free from Signs and Symptoms 3 Years or More
	per cent	per cent	per cent	per cent
I	50.0	16.7	0	0
II	28.5	14.5	0	0
III	13.3	6.7	0	0
Total	25.0	10.7	0	0

* Group I without metastases.
Group II with operable metastases.
Group III with inoperable metastases.

TABLE VI

PRIMARY HEALING AND THE HEALING AFTER ONE, TWO AND THREE YEARS IN 14 CASES OF CARCINOMA AND 4 CASES OF LYMPHO-EPITHELIOMA TREATED 1924–1927 INCLUSIVE BY THE NEW TECHNIQUE

Group*	Primary Healing	Free from Signs and Symptoms 1 Year or More	Free from Signs and Symptoms 2 Years or More	Free from Signs and Symptoms 3 Years or More
	per cent	per cent	per cent	per cent
Carcinoma I	66.6	66.6	66.6	50.0
Carcinoma II	100.0	100.0	50.0	50.0
Carcinoma III	0.0	0.0	0.0	0.0
Total Carcinoma	42.8	42.8	35.7	28.6
Lympho-epithelioma II	100.0	75.0	75.0	75.0
Total Carcinoma and Lympho-epithelioma	55.6	50.0	44.4	38.9

* Group I without metastases.
Group II with operable metastases.
Group III with inoperable metastases.

During the year 1930 altogether 8 cases of tonsillar carcinoma were treated, and all of these 8 cases have become primarily free from symptoms. Five of these patients had at the beginning of the treatment developed metastases.

Tonsillar sarcomas have been treated with a uniform technique since the year 1916, namely, external treatment with roentgen radiation 4 mm. Al plus 0.5 Cu filter, 30–40 cm. distance, and after the tumor had diminished, surface contact application of radium tubes was made with a filter equivalent to 1–2 mm. of lead, total dose 300–1700 mg-hr. of radium element. Of 35 cases of sarcoma treated during the period 1916 to 1927, inclusive, 15, or nearly 43 per cent, are living free from symptoms after three years, while the percentage of five year healing is almost 38 per cent (Table VII).

TABLE VII

PRIMARY HEALING AND THE HEALING AFTER ONE, TWO, THREE, AND FIVE YEARS IN 35 CASES OF SARCOMA, TREATED 1916–1927 INCLUSIVE

Group	Primary Healing	Free from Signs and Symptoms 1 Year or More	Free from Signs and Symptoms 2 Years or More	Free from Signs and Symptoms 3 Years or More	Free from Signs and Symptoms 5 Years or More
	per cent	per cent	per cent	per cent	per cent
I	100	77.8	77.8	77.8	77.8
II	91	75.0	75.0	66.7	44.4
III	36	7.1	7.1	0.0	0.0
Total	71.4	48.6	48.6	42.9	36.7

Group I without metastases.
Group II with operable metastases.
Group III with inoperable metastases.

Carcinomas of the upper jaw are likewise among those tumors where surgical treatment has produced comparatively poor results. Several surgical authors, Krönlein, Heyman and Sebilau, have had recurrences in nearly all the cases operated upon, and even the best surgical statistics show a healing percentage of only 20–25 per cent, as will be seen from Table VIII.

TABLE VIII

RESULTS OF SURGICAL RESECTION OF CARCINOMA OF THE UPPER JAW

	Number of Cases	Freedom from Signs and Symptoms	
		Per cent	Lasting for
König	48	16.6	5 years or more
Martens	79	20.2	5 years or more
Holmgren	39	25.5	5 years or more

Still during the years prior to 1922 all operable cases in Sweden were only operated upon. At the Radiumhemmet there were treated during this period consequently only inoperable cases and recurrences, as well as some few postoperative borderline cases. These were treated chiefly with external roentgen radiation as well as with implantations of radium into the cavity left by the operative procedure. But with the then prevailing surgical methods, we had great difficulty in exploring this cavity and consequently were unable to properly apply our therapeutic methods. The result of the radiation treatment is about equal at the different institutions, as is shown by Table IX.

At the Radiumhemmet freedom from symptoms for four years or more was attained in only 18 per cent of the cases. Nevertheless, it is impossible to draw any definite conclusions from the available statistics as to the five year healing because they are not complete.

Table IX

CARCINOMA OF THE UPPER JAW

Results of chiefly radiological treatment, with minor surgical interference

	Number of Cases	Freedom from Signs and Symptoms	
		Per cent	Lasting for
Quick	36	22	6–39 months
Johnson	24	20	1–5 years
Schreiner	46	10	1–9 years
Berven	44	18	4 years or more

Since the year 1922 several clinics have, to a large extent, been using a combination of total resection, with the ordinary surgical technique, or with endothermy followed immediately by the application of radium tubes of the open wound. At the Radiumhemmet we are now using the following technique: preoperative treatment with roentgen radiation, filter equivalent to 2.6 mm. Cu, 40 cm. distance. After the tumor has diminished in size, endothermy is performed with the method elaborated by Holmgren, and radium is applied in the wound, a total of 100–150 mg. radium element for 12–15 hours, filtered through 3 mm. lead. In early cases the preoperative roentgen treatment is not included.

At other clinics resection is done with the customary surgical technique, except by New, who uses endothermy. There are as yet not available any five year healing statistics, covering any very extensive material, but the percentage of healing for one to nine years is remarkably similar for all clinics, and amounts, by way of example, for Hautant to 38 per cent, for Barnes to 52 per cent (only cases without metastases), for Crosby-Greene to 33 per cent, for New to 36 per cent, and for Holmgren and the Radiumhemmet to 36 per cent (Table x).

According to Holmgren, endothermy plus radium is followed by a lower postoperative mortality (average 11–16 per cent, Holmgren 5 per cent, New 0 per cent), better cosmetic results and less shock from the operation. The drawbacks of endothermy are the longer operating time, and the longer healing period, with concomitant discomforts to the patients.

The glandular regions are treated at the Radiumhemmet with the same technique as all malignant tumors in the oral and nasal cavities.

Before the year 1924 the glandular regions were being treated with heavily filtered roentgen radiation, but we now make use of teleradium, because radium has, as stated before, been found to be superior to roentgen rays in the treatment of these regions.

In instances where at the beginning of the treatment no clinical glandular metastases exist, the patient is given only external teleradium treatment (5mm. lead equivalent filter, 6 cm. distance). In the majority of cases the teleradium treatment covers both the primary growth and the cervical lymph nodes.

In those cases where at the beginning of the treatment nonadherent clinical metastases exist, the patient is given teleradium treatment, as has previously been described. If the metastases disappear, such teleradium treatment is given in various

Table X

RESULTS OF COMBINED TREATMENT OF CARCINOMA OF THE UPPER JAW

	Number of Cases	Freedom from Signs and Symptoms	
		Per cent	Lasting for
Resection + Radiation (Hautant)	18	38	1.5–5 years
Resection + Radiation (Barnes)	25	52*	1–9 years
Resection + Radiation (Crosby Greene)	36	33	1–5 years
Endothermy + Radiation (New)	97	36	1–8 years
Endothermy + Radiation (Holmgren)	64	36	1–7 years

Postoperative mortality by surgical resection 11–16 per cent.

Postoperative mortality by endothermy 0 per cent (New)—5 per cent (Holmgren).

* Only cases without metastases.

series, with diminished doses for each series. If the metastases do not disappear, a dissection of the neck is made, with implantation of radium needles in the wound (10 mg. needles, filter equivalent to 1 mm. of lead, for 3 hours). In those instances, lastly, where a beginning fixation of the metastases exists, or in the case of inoperable metastases, only teleradium treatment or palliative roentgen treatment, with a tin filter equivalent to 2.6 mm. Cu is given.

CONCLUSIONS

1. In the radiation treatment of carcinoma of the oral and nasal cavities we are now using at the Radiumhemmet a combination of radium and endothermy for the treatment of the primary tumor, and a combination of radium and conservative surgery for the treatment of the lymph node bearing areas.

2. Radium has proved superior to the quality of roentgen radiation available at present.

3. The greatest gain of recent years in a therapeutic-technical respect has been the introduction of the teleradium technique and the more widespread use of the interstitial implantation of radium needles, in combination with endothermy.

4. Teleradium treatment enables an increase in the quantity and quality of the radiation, and in the tissue doses, factors which greatly augment the effective action of the irradiation.

5. The interstitial implantation of radium needles completes or supplements, in the various parts of the tumor, in the best possible manner, the dose given in the previous teleradium treatment.

6. Endothermy removes, without bleeding and without any risks of local re-implantation or spreading of the tumor, any resistant tumor remnants.

7. The treatment of the primary tumor consists routinely of an initial teleradium treatment which, after the tumor has become clean, diminished in size and better delimited, is followed by endothermy by simultaneous interstitial implantation of radium needles around the coagulated area.

8. The treatment of the lymph node bearing areas consists of the application of teleradium simultaneously with the treatment of the primary tumor. Surgical dissection is indicated after the teleradium treatment, if any movable easily operable glandular metastases remain. Otherwise only teleradium is used.

9. Of 278 patients suffering from carcinoma of the oral cavity (tongue, sublingual region, cheek and mandible) 75, i.e., 27 per cent, are free from symptoms from five to eleven years. Of 18 patients suffering from epithelioma of the tonsils 7, i.e., 39 per cent, are free from symptoms three years or more. Of 35 patients suffering from sarcoma of the tonsils 15, i.e., 43 per cent, are free from symptoms three years or more, and 38 per cent for five years or more. Of 64 patients suffering from carcinoma of the upper jaw 22, i.e., 36 per cent, are free from symptoms from one to eight years.

10. Radiotherapy should be practised in thoroughly equipped radiotherapeutic clinics with daily and intimate cooperation between scientists who are devoting themselves entirely to this work, namely, surgically trained radiologists, as well as physicists and pathologists.

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DISCUSSION ON PAPERS BY DRS. COUTARD AND BERVEN*

DR. JAMES EWING, New York City. It has been said that the progress of cancer treatment keeps pace with the progress of radiation. Certainly that appears to be true in the field discussed this morning. I look back over the years when surgery alone was employed in this field with emotions that are unpleasant. I look back also at the early days of the treatment of these diseases by radium and x-ray with little satisfaction. But this morning we have seen from each of these clinics a record of steady change, trial and error, improvements in this and that direction, with constantly increasing success, and when we hear, as we have heard from these three clinics, that from 20 to 38 or 40 per cent of tonsillar cases are now curable, we can accede to the statement that the progress of treatment of cancer in this field keeps pace with the progress of radiology.

Of the questions which might be discussed properly by a pathologist, it is interesting to observe how thoroughly these clinics are considering the great variation in the structure of the tumor, its natural course, the complications, because all these vary with different forms of tumors. The greatest importance of distinguishing grades of tumors is not perhaps so much in determining radiosensitivity, because that is a very complex general pathological and clinical question. It is of greater importance to call the attention of the surgeon and the radiologist to the natural course of particular types of tumors because we know that tumors of one type run a certain course and tumors of the same organ of a Grade 4 type run another course. Not only will your dosage of radium and x-ray be determined thereby, but the whole attitude toward the case will be much more intelligent and you will be able to save some patients useless misery and cure others, which you could not do intelligently without the knowledge of the natural course of the disease which depends essentially upon structure.

Dr. Coutard referred to the fact that the bed of the tumor in the laryngeal cases especially was a very important factor in determining radiosensitivity and the outcome of treatment. The more I attempt to unravel the numerous factors that seem to enter into radiosensitivity, the more I am impressed with the importance of the bed of the tumor. Some beds are vascular and give a good reaction. Others are bony and give none. Others are in the lymph nodes where things are very favorable. In mammary cancer, one of the great problems is to overcome the lack of reaction of fat tissue. Let me, following Dr. Coutard's lead, emphasize the importance of considering most carefully this particular factor in radiosensitivity.

Yet radiosensitivity will eventually be found closely related to what pathologists call differentiation in structure. If you throw that out, you capitulate entirely to the pessimists on this question of radiosensitivity.

A matter of first importance and of the greatest interest to me personally has been the question of dealing with neck nodes in intraoral carcinoma. I am very much gratified to see that Dr. Quick especially, and others also, have entirely cut loose from the old surgical dictum that block dissection of the nodes is essential for intelligent care of intraoral carcinoma. The results have not justified that contention at any time. Bloodgood reported that 65 per cent of the nodes that he excised in his cases of lip cancer were uninvolved and yet these extensive operations were employed, and are still em-

* A paper by Dr. Douglas Quick, Memorial Hospital, on "Principles and Methods Employed in the Treatment of Intraoral Epidermoid Carcinoma" was also read in this symposium. The discussion is included here and the article will be published in a subsequent number.

ployed. I saw recently from an authority of high standing a statement that today the treatment of choice of lip cancer is excision of the primary lesion and block section of the lymph nodes. We also know that some surgeons have gone so far as to develop that supersurgery which would dissect both sides of the neck from ear to clavicle without regard to the presence or absence of metastasis. Therefore, I think we can say that radiology has enormously increased the intelligence as well as the success of the treatment of these lymph nodes.

It would appear, at first sight, that the dissection of the neck and exposure of an obviously cancerous lymph node, implanting it with radium seeds and leaving the node in the neck must be unreasonable. The reasonableness will be determined by long experience. The reasons are not hard to find if one will cut those nodes microscopically in series and see what happens when you have a large cancerous lymph node in the neck. You will find, as a rule, that there is a marked regression of the tumor next to the capsule, where it often resembles normal skin, and a tendency in the majority of cases for the central portions to necrose and when you implant those nodes with a moderate amount of radium, you intensify that process and bring about a complete regression of the tumors, in many instances, and its transformation into an indolent epidermoid cyst; whereas when you attempt to dissect that node, the mechanical pressure almost invariably will squeeze cells through the capsule, out into the adjoining tissues, and then your recurrence is not in a lymph node, but in the cellular tissues and fat tissues, and every radiologist and every surgeon knows what a hopeless and dreadful condition results from such a complication.

I once tried in a lymph node in a case of cancer of the breast, about 1.5 cm. in diameter, to calculate the number of cells there were in that node, and the calculation was not a mere guess. It reached a little over 8,000,000,000, and yet you expect the surgeon to dissect that node out of its connections and get it out without disseminating any of those cells. Yet we have good theoretical reason to believe a very few of those cells implanted will produce metastasis. Therefore, I believe this highly conservative treatment of the nodes is based on sound pathological principle.

It was certainly a keen conception and a bold step when several years ago Dr. Coutard began to treat laryngeal cancer with heavy external irradiation. While the organ is, on the whole, accessible, the critical location of the tumors, the complications that naturally would arise as a result of heavy irradiation, held us all back and made it seem quite quixotic to attempt to cure these tumors by external irradiation. Yet step by step he has improved the technique and now we find that a high proportion of these laryngeal cancers are curable by external irradiation. We have followed the method at our institution with excellent results.

It is a splendid thing to think that nowadays an extensive carcinoma of the larynx, of the sinuses, at the base of the tongue or extending up even to the tonsil, may within a period of a month be caused to completely regress and remain cured by means of an external invisible agent.

Yet while admitting this important, permanent contribution, I feel that we should be cautious in submitting patients to measures which have a mortality and a considerable morbidity. Therefore, while welcoming this attempt to treat laryngeal and intraoral cancers by external irradiation alone, as a layman who sees these patients from the human side, I am not convinced that that is the way radiology is going to make its best and final progress in this field. The method is not applicable to every person. Many of these cases occur in elderly subjects. You have to pass them off because you know they won't stand it. The lesions are complicated. You must expect a tracheotomy in a good many of them.

Dr. Coutard, as a true scientist, has very frankly exposed in a chart the various complications which arise, which he interprets as hepatic and cardiac; he did not mention asphyxia or edema of the glottis, but all these things occur and they are of very great significance. Here we are dealing with major radiological problems. Therefore, from the point of view of a layman, I feel it would be well if you could in some way limit the amount of external radiation, the general body dose, and these very severe reactions of the skin. You could limit that part of the treatment and intensify it by some other method, either by applications of tubes, as Berven seems to have done, or by that desideratum which we are all hoping for, some method of increasing the effects of irradiation by constitutional agents, elevation of the temperature of the body or whatnot. I haven't the solution myself, but if in some way we could limit the amount of damage done to the local

tissues and to the body in general and intensify the effects of irradiation locally, then I think we shall be on much safer ground.

I trust that radiology, which makes its bid for consideration on the fact that it is humane, bloodless, and should be in many instances painless and far more effective, will not fall into the same difficulty that surgery finds itself in today, and will not be called upon twenty-five years from now to express regret at the severe conditions which we produce in our patients in the treatment of cancer. The penalty visited upon the cancer patient today is too severe, and I think it would be rather better not to attempt to cure so many cases if the standard methods of radiological treatment become so severe that there is a high mortality.

Dr. Francis Carter Wood, New York City. One cannot but be immensely impressed by these reports which show so definite a progress in the method of treatment of hitherto incurable types of neoplasms.

The first thing that is obvious from all three papers is the necessity of concentration of the cancer patients in institutions and not expecting good results by scattering radiation in inexpert hands. In other words, here are three clinics which have the facilities for the hospitalization of the patient, have concentrated a large number of patients so that high skill can be obtained by those who are treating these individuals. That such high skill is necessary, I think no one will doubt, because otherwise we would not have the records which have been reported this morning.

The second thing that appears in all the papers is the general recognition at the present time of the necessity of enormous dosage to obtain any permanent results. We are forced to give patients quantities of radiation which do produce serious symptoms from which those patients may not recover for a period of weeks, due to serious damage to the skin and mucous membranes, surgery in the form of the insertion of needles into or about growths, anesthesia—all in all, a combination of types of treatment, none of which is pleasant. It prevents our treating a certain number of patients by these techniques, because with the highly nervous, sensitive patient the carrying through of a course of heavy irradiation may be quite impossible. They will refuse to continue treatment long enough.

The recognition by all of the speakers of the importance of biopsies and the careful study of the microscopic structure of the tissues is an evidence of the importance of this factor in the treatment. The variety of the therapeutic attack, too, has been exposed this morning fully, the difference in attitude which exists, one clinic feeling that radium is far preferable to roentgen radiation and gives better results.

I heard Professor Forssell say in Paris that if he could get 20 grams of radium, he would welcome it and use it in preference to roentgen rays. On the other hand, in the Regaud Clinic, the two agents are regarded as equivalent under the conditions in which they are used, that is, of extremely high filtration with a careful timing of the exposures. Here is a factor which has been largely neglected hitherto, the question of the distribution in time of the dose. The original work which laid the foundation for this was in print in 1908 in publications of Professor Regaud's on the effects of radiation on animals where he showed that by prolonging the dose more effective sterilization of the tissues could be obtained than by giving a single large exposure.

The interest and benefits which we have received from Dr. Coutard's work are largely due therefore to the firm scientific foundation upon which all the work in the Radium Institute has been carried on.

I was very much interested in one point which Dr. Berven made, and that was that there was no improvement in the type of case coming to the clinic or the type of case which the clinic treated in carcinoma of the tongue, for instance; that the cases were more advanced in recent years than they were earlier. I wonder whether that is due to the patients feeling that they can get a cure without surgery, without coming quite so early, because they have heard of other patients being cured, or whether it is due to indifference of the medical profession, or upon what factor it depends. I hope that Dr. Berven will explain the point, because it is a very interesting one.

There was mentioned the risks of irradiation of cases with infection and the necessity for constant care of the patient, which is again another point as regards hospitalization of cancer patients in institutions where they can be properly treated.

Syphilis was not spoken of as one of the deterring factors. In carcinoma of the tongue, very unfortunate results are not infrequently observed in the syphilitic, despite energetic antisyphilitic treatment immediately preceding

the treatment. Probably this is due to the permanent damage which syphilis causes on the vascular system and with the combined vascular damage which results from irradiation, large sloughs and serious, if not fatal, infections may easily result.

The whole meeting this morning has been a demonstration of the importance of the scientific foundation of individual groups of men working on plans which they have formulated. I hope that five or ten years from now the same clinics will report and we will have perhaps statistics based upon the different techniques which have been illustrated here this morning, giving a larger material and furnishing some evidence of the final codification of our therapy which is necessary in irradiation. We must establish ultimately certain specific types of treatment for a given lesion. Now one radiologist uses one filtration and another uses another, and a third uses radium alone, and the fourth uses diathermy, and the fifth uses surgery. It is necessary in the next few years to determine in this group of lesions which are attackable by irradiation, just what that irradiation shall be, the type, and what is the direction in which we are to go in the future.

DR. A. U. DESJARDINS, Rochester, Minn. On listening to these three important communications, I have been impressed chiefly by two points. One is that the three institutions represented are working under special circumstances and conditions and, therefore, similar results cannot be expected or hoped for under the totally different conditions which exist in the practice of the private radiologist or of ordinary hospitals. Dr. Wood has already mentioned one of these points and stressed the importance of concentrating means and facilities for such treatment in specially equipped institutions with highly trained personnel.

The next point is that methods of this kind are totally different and cannot possibly be reconciled with any idea of standardization. The two ideas are at opposite poles. The methods described must be fitted carefully and painstakingly to each patient; otherwise, comparable results cannot possibly be attained.

DR. IRA I. KAPLAN, New York City. It is difficult to have very much to say after so many eminent men have spoken upon these subjects, but I think a few important factors might be brought out. One of these is that no matter what type treatment had been given in any of these clinics, the results have been practically the same. We must not draw conclusions from this fact that you can use any one of these methods and get good results. An important factor in this whole matter is that each one of these three men who spoke here this morning is essentially a clinical radiologist, that all this work has been done in a clinical manner, and, as Dr. Quick has carefully brought out, you have to use clinical judgment in whatever method you employ. It doesn't make any difference whether you use surgery in the open or closed method, or whether you use endothermy or radiation, you have to judge which upon clinical facts.

The second great important factor which all three men brought out is that you have to use a planned method of taking care of these cases. In my service, I have the good fortune or perhaps the bad fortune, to have a hospital where we get all types of hopeless cases already treated by every kind of method. It has often come up in my mind, "Why do these failures exist? Is it the patients? Is it the man or is it the method?"

I think the great point in these failures is the fact that the patients have been treated without a prepared plan or clinical judgment. Those who are radiological clinicians fail sometimes, but the ones who aren't clinicians fail more often.

Dr. Coutard brought out the important factor of using heavy dosage in irradiation, and we have Dr. Quick's warning that we do not know as yet whether or not this heavy dosage is the proper factor to employ in every case.

Dr. Coutard called our attention to the fact that a certain limit is necessary, that if he goes beyond 8,000 r he gets no better results.

Dr. Berven has shown us that it is necessary to have a very definite follow-up in the care of cases, and it is only because he has this excellent follow-up that he is able to judge whether to repeat his method in caring for these patients. Whether or not endothermic surgery is better than scalpel surgery, I think depends upon the man using the method. A good surgeon with a clean scalpel can do a great deal of good work. A poor surgeon with the finest of endothermic instruments can't do anything at all.

All three clinics have shown this fact that we must have proper irradiation carried out in centralized units, and that we must use a clinical understanding in the care of patients. I think the day is past when the radiologist without clinical knowledge or a clinician without

radiological experience can care for cancer patients.

DR. GEORGE E. PFAHLER, Philadelphia. I am sure that we all appreciate the instruction given to us this morning by these great leaders. We must also be impressed, all of us, with the tremendous reaction brought about by the treatment given by Dr. Coutard. Yet Dr. Coutard has used in this treatment, you will remember, 2 mm. of zinc, which is approximately equivalent to 2 mm. of copper. You will find that most radiologists are working with 0.5 mm. of copper. That difference is a very great one from the end-results and yet in spite of the fact that increased filtration was used, Dr. Coutard used a dosage there that would be very difficult for us to carry out in any routine manner in this country. We would run into many law suits for x-ray burns. On that account and because of the fact that I am convinced, as Dr. Berven is convinced, that radium will produce a greater relative effect upon the cancer tissue, I have favored the use of radium filtered through 2 mm. of platinum, equivalent to about 4 mm. of lead. That increases the filtration even more and, therefore, gives relatively less damage to the soft tissues.

I think another point that must be emphasized is that each case must be treated as an individual and not according to any rule. That is, of course, what all these men have been doing. You will see that Dr. Quick, in certain cases, excises the glands; in other cases, he opens the skin and introduces seeds into the gland that cannot be removed. Dr. Berven removes remnants of disease by means of electrocoagulation or the endothermy knife, which is a method that must also be adapted to the individual. We cannot lay down specific rules or we will get into a lot of trouble.

Another point I would like to emphasize that Dr. Berven brought out is that when he introduces radium after this removal of the remnant of disease, he doesn't leave his radium, his 10-mg. radium needles in there for a very long time, approximately three hours. These are facts that we must keep in mind or we will get a bad necrosis and a bad healing.

DR. BERVEN (closing). I would first answer Dr. Wood who asked me a question: I get about the same results of healing with the first method, during the roentgen period, 32 per cent, five years healed, as with the radium. I get the same per cent of healing. It depends upon this fact, which is very well known, that all clinicians get their patients referred from doctors all over the country. The doctors usually think, "This case is too bad to send to the Radiumhemmet." So when we begin to treat patients, we have the good cases. Then we treat them and we accomplish our results; we read our papers at the societies and meetings, and we tell the doctors, "You shall send more patients." Of course, they are coming in a greater number, and in more advanced stages of the disease. We have to accept all these patients and treat them, or try to treat them. It is impossible for us to cure all these patients; to some we can give only palliation.

Therefore, it is a well known fact, as you know, in all clinics that when you have published good results of a treatment, afterwards you get more advanced cases and you can't show such good results.

I will say a few words about Coutard's method. Since his first communication in 1928 at the Second International Congress in Stockholm, where he published his original method of treating malignant epitheliomas of the tonsil, this method has interested the whole radiological world. We have not heard from Coutard since 1928, and I think that it is now of the greatest importance that Coutard has published a more detailed paper. The paper would, of course, have been of much greater value if the detailed histories had followed it to illustrate the many different variations in the technique.

Coutard has tried to elaborate a method of treatment by roentgen rays which gives the reaction of epidermitis, epithelitis and dermititis without damaging seriously the surrounding tissues. His method gives a violent primary reaction of the mucous membranes and of the skin with severe pain and considerable discomfort to the patient. He gets some late necrosis, but in most cases he has obtained very, very good results.

I have seen many patients treated with his method and I have also treated patients with it and if I compare the reaction that I get following Coutard's method, the roentgen treatment and the radium treatment, that reaction after the radium treatment is much lighter for the patient. If does not cause so much pain and I see in my practice no deaths from the radium treatment. In our opinion, that depends upon the different wave lengths, the short wave lengths of the gamma rays.

I have been in many clinics and I have heard

doctors say, "We use Coutard's method," but it has been very difficult to really use Coutard's method from the short account published in 1928. In my opinion, I have not seen any place where the real Coutard method is employed. I have seen some modifications of his method. Therefore, I am glad that we have a more detailed report now, because Coutard's real method cannot be responsible for all the bad results which have followed the technique supposed to be Coutard's.

There has been only one paper published from one clinic, the clinic in Zurich, where the doctors have used Coutard's method and try to use it. They said, "We attempt to do it, and we think we have come near his method, but the results have been very bad." They treated seven patients and of these seven patients, only one of carcinoma of the tonsil, epithelioma of the tonsil, was free from symptoms and living after one year. The other six died, and three of them died directly from injuries from the treatment.

The different results with the same technique show, in my opinion, and I think in the opinion of most of us today, that the primary healing as a permanent cure depends not only upon the perfection of the technique and the manner in which it is employed, but also on other requirements. The results that Coutard has obtained, I think depend upon himself. He follows his patients very carefully. He examines his patients at least twice a day. He follows their general condition and he knows what injury he causes and he knows what reactions come from the treatment.

The indications for the treatment, as well as the carrying out of this treatment, are yet so complicated that we cannot look upon Coutard's method as a method for use in general roentgen practice, but the further development of this method, as well as the development of the radium method, must be carried out at the large special clinics.

I am so glad to have heard this morning from the doctors discussing these papers that they appreciate the value of the clinics for treatment of malignant disease. As I said in the beginning of my paper, it is a bad, bad method to allow radium to go out to doctors in small quantities to be used by doctors who see only some few patients during the year. It is impossible for them to get the experience in doing this work sufficient to treat patients, and it is impossible for them to follow up the cases and know their results.

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ROENTGENOLOGIC EVIDENCE OF FETAL DEATH*

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MÜLLERHEIM in 1899 reported a case in which he had been able to demonstrate the fetal skeleton on a roentgen plate, and in 1912 De Lee,[32] enumerating the possibilities of the roentgen ray in obstetrics, prophesied that eventually fracture of the fetal skull in utero might be diagnosed, but the possibility that roentgen rays might be of assistance in diagnosing fetal death in utero was apparently not thought of until 1921. In December, 1921, Horner,[22,23] and in April, 1922, Spalding[38] independently read papers on this subject, and since that time a fairly extensive but somewhat conflicting literature has arisen.

In the present paper we shall review briefly the clinical signs of fetal death, discuss the gross pathology of the still-born fetus and then outline the published views of others on the roentgen findings in this condition. Following this we shall present our own studies on the roentgenograms of 176 pregnancies, in 14 of which the fetus proved to be dead, and (based on this) our conclusions as to the value and validity of a roentgen diagnosis of dead fetus.

CLINICAL EVIDENCE INDICATING LIFE OR DEATH OF FETUS

Certain clinical signs and symptoms are recognized as useful in diagnosing fetal death, but the fact that so many are listed is evidence that no one is thoroughly reliable. Syphilitic infection of the father or mother, acute or chronic nephritis in the mother or habitual death of the fetus from unknown causes are factors that support a clinical diagnosis of fetal death. The subjective symptoms of disappearance of fetal movements, languor, malaise, chilliness, foul taste in the mouth, sensation of weight in the abdomen and loss of weight of the mother are at best presumptive evidence.[35] Flabbiness and arrested growth of the breasts are suggestive and even more so are the sudden cessation of nausea and vomiting in the early months of pregnancy, a discharge of bloody liquor amnii or milky fluid from the vagina,[10,11] and improvement in cases where toxemia has been present.[1a]

Maternal consciousness of fetal movement is strongly suggestive evidence of fetal life, whereas the absence or cessation of such consciousness suggests death. Szellö,[48,49] however, voices the general obstetrical opinion when he points out that demonstrably live fetuses frequently undergo periods of quiet and that, conversely, it is not particularly uncommon for women to interpret movements of the maternal intestine as fetal movement.

Recognition of fetal movement by the palpating hand of the physician or by auscultation supplies quite dependable evidence of fetal life. However, movements of maternal muscles may be misinterpreted as fetal activity. Absence of fetal movements means little unless it is noted at several examinations.

Drosin,[16] in 1922, described two clinical procedures calculated to induce vigorous fetal movement and thus establish definite proof of life. In the first, the recumbent patient exhales and suspends respiration for as long a time as possible. The resulting anoxemia frequently stirs up the desired movement of the fetus. The second consists in pressing the finger tip firmly against the anterior shoulder of the fetus.

Absence of the fetal heart tones, while extremely important, is not invariably reliable. In prematures the heart tones may be too weak to be heard and even in the full-term fetus they may be imperceptible because of position, fat abdomen, edema,

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excess of liquor amnii, distended bladder, intestinal gas, accumulation of feces or because of contractions of the uterus, the action of the abdominal muscles or other extraneous noises. Anterior implantation of the placenta and uterine souffle are apt to interfere with fetal heart tone auscultation (Drosin[16]). Two physical signs are considered absolutely diagnostic of fetal death. One called by Szellö[48] "the first sign" is the absence of pulsation in the umbilical cord as it is palpated digitally in the uterus. The maneuver is obviously seldom possible during gestation. The second sign, described by De Lee,[10] Williams,[55] Quin, [35] Speidel and Turner,[43] and others, and designated by Szellö as "crepitatio ossea," consists of palpation of a macerated head through the abdomen, vaginal fornix or cervical canal.

Disproportion between the size of the uterus and the estimated duration of pregnancy is suggestive of fetal death.

Baer has noted that the increased basal metabolic rate normal to pregnancy is absent when the fetus is dead, and Stein and Arens[47] consider the sign rather significant.

De Lee and Guiranden[10] note that the clotting time of the maternal blood may be reduced to less than five minutes when the fetus is dead.

According to Cohnstein and Fehling the temperature of the uterus is higher than that of the vagina late in normal pregnancies, the difference disappearing if the fetus dies. This evidence is often helpful, but Szellö believes that the danger of breaking the thermometers makes the procedure impractical.

Attempted induction of labor by means of drugs may be used as a therapeutic test when fetal death is suspected. It fails if the fetus is living and usually succeeds if the fetus is dead.[1a]

THE PATHOLOGY OF THE MACERATED FETUS

Still-birth or the death of a human fetus on or after the twenty-eighth week of intrauterine development may be due to any one or any combination of many causes, but whatever the cause the dead fetus assumes the rôle of a foreign body and suffers catabolic changes that have been called maceration. There is early autolytic decomposition in the abdominal viscera and petechial hemorrhages occur in the pericardium, pleura and peritoneum with resulting collection of decomposed blood in the body cavities (Magner,[27] Browne[6]).

The great fontanelle lengthens out to as much as 2 to 3 centimeters. The skull becomes smaller than it was during life and as a result there is wrinkling of the scalp. Spalding, and Portes and Blanche[34] attribute the change in size of the skull to a collapse and shrinking of the cerebral substance which results in an overlapping of the skull bones. Moss[31] states that the overlapping and shrinkage are due to "absence of some of the cerebral fluid." Newell[46] feels that the entire process is "due to the desiccation of the fetus after maceration has begun." Spangler[40, 41] believes that the overlapping is due to an increase in intrauterine pressure, similar to that seen in the beginning of labor. Albano,[2] on the other hand, is sure that the disturbed contour is not the result of pressure.

It has been asserted by some[34, 48] that the bones slowly lose their calcium so that if the fetus remains in the uterus long enough after death, it becomes almost completely decalcified. Opinion is not unanimous on this point, however.

ROENTGEN APPEARANCE OF THE SKELETON OF A DEAD FETUS

There are reported instances of roentgen diagnosis of pregnancy very early in gestation by visualization of the enlarged uterus or the fetal tissues by the aid of positive or negative contrast media.[45] Freund[17] in 1905 was of the opinion that the fetal skeleton could not be shown consistently until the second half of pregnancy, and while the development of the moving grid by Potter, and other technical advances of the past twenty-five years make possible occasional excellent roentgenograms of fetal skeletons

at three and one-half months, the fact remains that only in the second half of pregnancy are the results consistently good. Bartholomew has called this roentgenographic demonstration of a fetal skeleton "the fourth positive sign of pregnancy."

It is obvious that the detailed roentgen appearance of the skeleton of a particular living fetus is a function of fetal age, maternal build and numerous technical factors. Nevertheless, it is reasonable to suppose that the pathological changes ushered in by fetal death might produce significant alterations in the roentgenogram. As a matter of fact, five such signs have been described:*

1. Roentgenographic demonstration of overlapping of the skull bones with asymmetry of the head was reported by Horner[22] in 1921 as unique and positive evidence of fetal death. The same sign was described independently by Spalding[38,39] in 1922. The condition was explained as due to disproportion between the size of the skull and its contents incident to post-mortem shrinking of the brain. These two original publications were followed by many reports confirming the value of the sign, among which may be mentioned Portes and Blanche, Delherm and Morel-Kahn, Hauch, Recareus, Carreras and Faixat-I. Figueras,[9] Schochaert, Laffront and Viallet, Henrotay,[20] Tengbergen,[50] Szellö, Jungman,[24] Kehrer, Quin, Browne and Kincaid[7] and Schmitt.[37] Walton,[54] Doub,[15] Spiedel and Turner,[42,44] Bourland and Spangler,[5] Williams, Campbell and Willets,[8] and Matthews found the sign useful under certain conditions. On the other hand, Stein and Arens[47] in 1926 and Perry[33] in 1927 discredited the sign as pathognomonic and felt "entirely at sea" in attempting to diagnose fetal death on this evidence. Dorland,[12,13,14] Greenhill[18,19] and Willets[56] state that under certain conditions they consider the sign valuable.

Horner has nothing to say of possible confusion with the molding of labor and though Spalding mentions the matter, he feels that the appearance produced by labor is quite different from the overlapping of fetal death. Tengbergen also is of the opinion that overlapping due to shrinkage of the brain in maceration bears little or no resemblance to the molding of labor. On the other hand, Adair,[1a] Szellö, Matthews and many others are convinced that labor, or even engagement of the head may produce molding that cannot be differentiated from the overlapping of fetal death. (In passing, we agree with this.)

Shrinking of the brain does not occur immediately after the death of the fetus, so, of course, overlapping of the skull bones does not occur at once. Matthews[28] has reported the sign two to three days after the supposed date of fetal death and he believes that it is regularly present by the fourth day. Stein and Arens do not expect to see the sign until five days after death. Most workers agree that films must be of good technical quality and that stereoscopy is a valuable aid.

2. Jungman[24] in 1928 described a lordosis of the caudal half of the fetal spine, and Matthews[28,29] independently made the same observation two years later. Baumann[4] and Naujoks[24] have reported cases showing this sign, and Henrotay[20] has described the phenomenon as probably due to a loss of muscular tone in the lumbosacral muscles, as a result of which the fetal trunk appears to be "sunken together." Some workers[24,28] agree with Jungman in considering angulation significant only when it appears at the caudal end of the spine. Others[4,25] attach significance to angulation of any part.

3. Collapse of the thoracic cage has been listed by Matthews[28] as a roentgenographic sign appearing about two weeks after fetal death.

* In addition to these, Bourland and Spangler,[5] Kehrer,[26] and Matthews,[28] have described respectively, "flattening of the transparietal arch," "a sac-like distortion of the head" and "wrinkling of the fetal scalp" as supposedly earlier signs of the overlapping of skull bones. It is our opinion that all three are difficult if not impossible to make out and at best are merely slight variations in the appearance of the same underlying pathologic process—brain shrinkage. Kehrer[25,26] speaks of a peculiar position of the fetal arm elevated behind the occiput, thought to be due to rigor mortis and therefore significant of fetal death, but he does not illustrate the condition; it is not described by others and has not been seen by us. The extremities of living fetuses can and do assume such a variety of positions that we can scarcely imagine a position peculiar to death.

4. Tengbergen[50] and Henrotay point out that a fetus disproportionately small for the duration of pregnancy is probably dead.

5. Portes and Blanche in 1924 described faint visualization of the fetal skeleton which they believed was due to decalcification and others[20,48,58] have published supporting evidence. It is well recognized, however, that many technical factors affect the density of the skeletal shadows and Albano[2] feels that all faint shadows encountered after the date when the fetal bones should contain considerable calcium are to be explained on technical grounds.

TABLE I

CHRONOLOGICAL DISTRIBUTION OF CASES

Approximate Age of Fetus at Time of x-ray Examination		3 1/2 Months	5 Months	6 Months	7 Months	8 Months	Term	
Number in cephalic presentation		0	1	6	9	40	70	LIVE
Number in breech presentation		1	2	1	1	6	11	LIVE
Number of twins	Cephalic	0	0	0	0	0	6	LIVE
	Breech	0	0	0	0	0	2	LIVE
	Combined	0	0	1	0	3	2	LIVE
TOTALS		1	3	8	10	49	91	162
Number in cephalic presentation		1	1	0	3	1	1	DEAD
Number in breech presentation		0	2	2	0	1	1	DEAD
Number of twins combined presentation		0	0	1	0	0	0	DEAD
TOTALS		1	3	3	3	2	2	14

NATURE OF OUR MATERIAL

Our material consists of roentgenograms and clinical records of 176 cases of pregnancy examined at the Chicago Lying-In Hospital, for the most part during the eighteen-month period, January 1, 1930, to July 1, 1931.*

Twenty-one additional cases had been examined by roentgen ray but were omitted from the study because of incomplete clinical records or for other reasons. These 176 cases in which roentgen examination has been done constitute, of course, but a small fraction of all the pregnancies seen in the institution during this period and, unfortunately, include only 14 out of the 100 or more still-births recorded during these months.

DISTRIBUTION OF CRITERIA AMONG OUR CASES

Three of the 14 cases in which the fetus was dead are roentgenographically normal

* A few cases from Billings Hospital and at earlier and later periods have been included.

but the other 11 present two or more of the criteria that have been advanced as evidence of fetal death. The skull bones are overlapped in 3 cases, the spine is angulated in 7, the thorax is collapsed in 2 (questionable). Disproportion and a faintness of shadow which we interpret as decalcification are present in 7.

Of the 162 cases terminating in the delivery of a living fetus (including one not yet delivered but known to be alive) 15 were in labor at the time the roentgen examination was made. Of these, overlapping of the skull bones was present in 4, angulation of the spine in 5, while 7 showed no changes of any sort. Of the 147 cases not in labor, 9 showed skull changes that might be interpreted as overlapping, but no other criteria; 17, though presenting normal skulls, showed angulation of the spine.

TABLE II
DISTRIBUTION OF CRITERIA AMONG OUR CASES

	OVERLAPPING SKULL BONES (Horner, 1921) (Spalding, 1922)	ANGULATION OF SPINE (Jungman, 1928) (Matthews, 1930)	COLLAPSE OF THORAX (Matthews, 1930)	DISPROPORTION (Tengergen, 1926) (Henrotay, 1931) FAINT SHADOW (Decalcification?) (Portes and Blanche, 1924)	NO CRITERIA PRESENT
Fetus dead; patient not in labor (14 cases)	3	7	2(?)	7	3
Fetus alive; patient in labor (15 cases)	4	5	0	0	7
Fetus alive; patient not in labor	9 (All pseudo)	17 (Identical with that seen in death)	0	0	121

ABSTRACTS OF 14 CASES IN WHICH THE FETUS WAS BORN DEAD*

CASE I (Unit #38852, X-ray #17580) (Figs. 1A and B, and 11A). C. C., aged twenty-one. Para 1; weight 147 pounds; Wassermann negative. Onset of last menstruation, December 27, 1930. Predicted term, October 4, 1931.

May 7, 1931. Fetal heart tones not heard. Examination suggests four and one-half months' normal pregnancy.

October 6. Uterine size suggests six and one-half to seven months' pregnancy, macerated fetal head palpated.

October 7. Roentgen findings: Single fetus in cephalic presentation. Age estimated from occipito-frontal diameter, six months. Frank overlapping of skull bones and partial decalcification of skeleton. Angulation of caudal end of the spine seen only in the lateral view.

October 8. Medical induction followed by delivery of macerated fetus judged to be of twenty-eight weeks' development.

Note. Estimated from menstrual history, gestation was a little beyond term on October 7. If the roentgen estimate of fetal age is correct, this indicates a fetus dead three months at the time the film was made.

CASE II (Unit #77633, X-ray #325) (Fig. 5). G. F., aged thirty, Para 11; weight 167

* Most of the cases were examined before we became interested in the roentgenographic estimation of fetal age and the diagnosis of fetal death. These abstracts contain therefore not the original roentgen reports (many films had not been reported formally) but instead our present interpretation of what the films show. We have taken care to do this film reporting on the basis of the film findings alone uncolored by clinical knowledge of the case.

pounds; Wassermann negative. Onset of last menstruation, June 2, 1929. Predicted term, March 9, 1930.

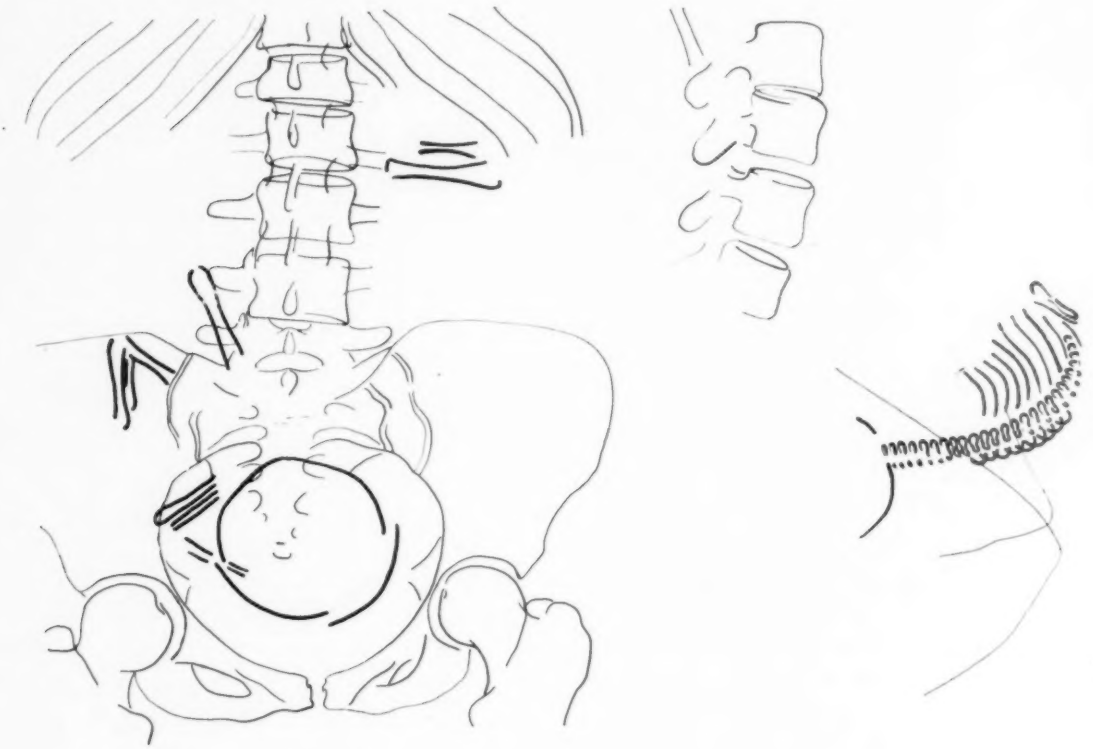
April 5. Fetal heart tones normal. No fetal movement felt after April 9.

April 11. Fetal heart tones absent.

April 14. Roentgen findings: Single fetus in cephalic presentation. Skull bones overlapped—spine angulated. Age estimated from occipito-frontal diameter nine months.

April 17. Difficult manual extraction of macerated fetus. Probable fetal age not stated. Time elapsed between probable date of fetal death and time of roentgen examination—five days.

CASE III (Unit #81820, X-ray #11876) (Fig. 11B). P. A., aged twenty-six. Para II; weight 188 pounds; Wassermann negative. Onset of last menstruation February 16, 1930. Predicted term, November 23, 1930.



A B

FIG. 1. A. Film tracing from Case I.* subject in supine position. Dead fetus showing overlapping of skull bones. Judging from the date of onset of last menstruation, pregnancy should be at term but the roentgen estimate of age is six months. This disproportion strongly suggests a diagnosis of fetal death. B. Film tracing from same case, subject in lateral position, showing a second criterion of fetal death, angulation of the caudal end of the spine.

September 8, 1930. Small amount of bloody vaginal discharge.

October 26, 1930. Active fetal movements. (Cannot determine from record whether this is objective finding by examiner or subjective sensation reported by the patient.)

October 31, 1930. Fetal heart tones not heard. Impression: Breech presentation or monstrosity.

October 31, 1930. Roentgen findings: Single fetus in breech presentation, age estimated from occipito-frontal diameter, six and one-half months. (Now that we know that hydrocephalus is present, possibly would estimate

* The points of interest on the film are outlined with a wax pencil. This outline is transferred to architects' tracing paper, inked with drawing ink, and then photographed. We have been careful to make wax pencil marks only where definite roentgen shadows exist. The fetal parts have been inked heavier than maternal parts to facilitate study of the tracings. It was obviously impossible to illustrate decalcification. Some of our films could have been reproduced by the half-tone method; many could not. The original films were displayed at the meeting of the Chicago Gynecological Society, January 15, 1932.

even younger fetus.) From menstrual history, pregnancy at eighth month. There is therefore disproportion, suggesting that the fetus has been dead for one and three-fourths months. The fetal skeleton appears partially decalcified. November 2, 1930. Delivery of macerated hydrocephalic fetus.

Note. If the notation of active fetal movement on October 26 refers to findings at palpation by an examiner, we are forced to the conclusion that the fetus had been dead for only five days on November 2 and that its small size was due to maldevelopment during life rather than the retention of a fetus dead one and three-fourths months. We doubt the likelihood of this; we believe that the fetus had been dead for one and three-fourths months.

Case IV (X-ray #10613) (Fig. 10D). E. K., aged twenty-six. Para 1. Onset of last menstruation, January 1, 1930. Predicted term, October 8, 1930.

August 8, 1930. Referred for consultation because no fetal movement had been felt for past two months. Examination showed uterus of about six months' size. No fetal heart tones. Maternal breasts small. No fetal parts could be palpated. Impression: Dead fetus.

August 8, 1930. Roentgen findings: Single fetus in breech presentation—age estimated from occipito-frontal diameter, four and seven-eighths months. Skull outline irregular but no frank overlapping.

August 15, 1930. Roentgen findings: Breech presentation—age estimated from occipito-frontal diameter, four and seven-eighths months. Angulation of thoracic spine. Decalcification.

Later in August, 1930. Delivery of dead fetus outside the institution. Exact date of delivery, estimated age, degree of maceration not recorded.

Note. Gestation, estimated from menstrual history, was of seven and one-fourth months' duration on August 15. We believe, therefore, that the fetus had been dead two and one-fourth months at that time. It is gratifying to note that occipito-frontal diameter measurements were identical in the two films made a week apart, in spite of the technical factors that might have been expected to introduce an error. In this case the clinical guess as to the time of fetal death coincides exactly with the calculation made from the roentgenogram.

Case V (Unit #80109, X-ray #10436) (Fig. 11C). M. S., aged thirty-two. Para II; weight, 149. Onset of last menstruation, December 2, 1929. Predicted term, September 9, 1930.

July 29, 1930. Clinical diagnosis: "Fetal death." Basis of diagnosis not recorded.

July 29, 1930. Roentgen findings: Single fetus in cephalic presentation—age not estimated. Skull obscured by maternal pelvic bones. At first sight suggests anencephalic but on closer study skull bones are present, grossly overlapped as a part of gross disorganization. Impossible to measure occipito-frontal diameter for age estimation. There is marked decalcification.

August 12, 1930. Roentgen findings: Special views attempted with hope of better visualization of skull. Still cannot estimate occipito-frontal diameter. Age estimated from length of femur, six and one-half months. Spine not angulated.

August 15, 1930. Spontaneous delivery of macerated fetus, probably of five months' development. Fetus, placenta and membrane delivered as an intact mass.

Note. Estimating from menstrual history, gestation was at eight and one-eighth months on August 12, so the roentgen estimate of fetal age indicates that the fetus had been dead one and five-eighths months when the film was made.

Case VI (Unit #82653, X-ray #12564) (Fig. 11D.). G. W., aged thirty-one. Para II; Wassermann negative. Onset of last menstruation, May 23, 1930. Predicted term, February 30, 1931.

December 16, 1930. Fetal heart tones not heard.

December 19, 1930. Fetal heart tones not heard. Painful uterine contractions. On rectal examination breech presentation, no skull crepitation made out, estimate uterus about six months' size.

December 18, 1930. Roentgen findings: Age estimated from occipito-frontal diameter, five and three-eighths months. Single fetus in breech presentation. Note also decalcification, angulation of caudal end of spine and possibly

thoracic collapse. Overlapping not seen but skull poorly visualized.

December 20, 1930. Spontaneous delivery of a macerated fetus thought to be dead about six days.

Note. Estimating from menstrual history, gestation was at six and five-eighths

FIG. 2. Film tracing from Case XV, subject in prone position. Live fetus at term with overlapping of skull bones due to labor. Roentgen estimate of age (over term) corresponds well with the known clinical facts. Compare with Figure 1, where gestation is also of nine months' duration but fetal skull is extremely small, indicating that the fetus died at the sixth month of development.

months on December 18. Assuming that the roentgen estimate of fetal age is correct, the fetus had been dead one and one-quarter months when the film was made. Against this interpretation we have the guess of the physician who conducted the autopsy that the fetus had been dead only six days on December 20.

CASE VII (Unit #82782, X-ray #11606) (Figs. 7 and 11E). G. L., aged twenty-seven. Para V; Kahn test negative. Onset of last menstruation April 19, 1930. Predicted term, January 26, 1931.

December 4, 1930. Fetal heart tones normal. Estimated development of fetus, eight and one-half months.

December 18, 1930. Fetal heart tones not heard.

December 18, 1930. Roentgen findings: Single fetus in cephalic presentation—age estimated from occipito-frontal diameter, six and seven-eighths months. Decalcification of skull makes statement on overlapping impossible. Spine angulated in cervical and thoracic region. Thorax collapsed?

December 26, 1930. Roentgen findings: Skull visualization still poor. Age estimated from occipito-frontal diameter, seven months.

December 27, 1930. Spontaneous delivery of macerated fetus thought to be dead seven to nine days. Thorax appears normal.

Note. Estimating from menstrual history, gestation was of eight months' duration on December 26. The roentgen estimate of a fetal age of seven months would indicate that the fetus had been dead one month on December 28. This is in conflict with the pathologist's guess of nine days. On the other hand, the clinical evidence favors the idea of death twenty-four days before December 26.

CASE VIII (Unit #82609, X-ray #12522). A. K., aged twenty-one. Para II; Wassermann negative. Onset of last menstruation, August 15, 1930. Predicted term, May 22, 1931.

October 16, 1930. Clinical findings suggest possibility of ectopic pregnancy.

December 15 and 16, 1930. Roentgen findings: At first no evidence whatever of fetal parts, but on re-examination after administration of enema irregular oval mass of densities in region of rectal ampulla interpreted as a very small macerated fetus with partly disorganized skull bones. Age estimated from occipito-frontal diameter, three and three-fourths months. Overlapping probably present but skull so small, visualization so poor because of overlying sacrum, unwilling to classify as overlapping. Following this (exact date not available—patient not in the hospital) there was abortion of a fetus judged to be approximately four and one-half months old.

Note. Estimating from the menstrual history, gestation was of three and three-fourths months' duration on December 16, 1930. Assuming the age estimation from

the roentgenogram to be accurate, the fetus was alive or very recently dead at the time the roentgenogram was made.

Case IX (Unit #82712, X-ray #12523) (Fig. 11F). L. H., aged eighteen. Para 1; Weight 111; Wassermann negative. Onset of last menstruation, April 17, 1930. Predicted term, January 24, 1931.

November 3, 1930. Fetus active.

November 24, 1930. Fetus active.

December 15, 1930. No activity of fetus. Fetal heart tones hot heard. Brown vaginal discharge. Question of palpable uterine myoma.

December 15, 1930. Roentgen findings: Single fetus in breech presentation—age estimated from occipito-frontal diameter, five and one-half months. Decalcification but no angulation of spine, collapse of thorax or frank overlapping of skull bones.

December 21, 1930. Abortion of a macerated hyrocephalic fetus thought to be of about six month's development.

Note. Estimating from the menstrual history, gestation was of seven and three-fourths months' duration on December 15. Assuming the roentgen estimate of fetal age to be correct, this would indicate a fetus dead two and one-quarter months at the time the roentgenogram was made. The history notes of fetal activity on November 3 and November 24 suggest that our estimate of the period of death is a little too long. If these history entries refer to maternal impression of fetal movement they may not be dependable.

Case X (Unit #82913, X-ray #12688). B. P., aged forty. Para VIII. Onset of last menstruation, July 15, 1930. Predicted term April 22, 1931.

December 30, 1930. History of abdominal pain of six weeks' duration. Recent rapid increase in abdominal size. Nausea, vomiting, bloody discharge. Physical examination: Suspect five to six months' pregnancy, possibly twins, possibly polyhydramnios. Fetal heart tones not heard. Believe fetus dead.

December 31, 1930. Roentgen findings: Two fetuses are present. Age estimated from occipito-frontal diameter, four and seven-eighths months. One lies in cephalic presentation, the other is transverse. The outline of the uterus is quite well seen and there is apparently a great excess of fluid. No overlapping of skull bones, angulation of spine, decalcification, etc.

January 1, 1931. Spontaneous delivery of dead twins thought to be of about five and one-half months' development. Marked excess of amniotic fluid.

Note. Estimating from the menstrual history, gestation was of five and three-eighths months' duration on December 31. Assuming the roentgen estimate of age to be correct, the fetuses had been dead half a month at the time the roentgenogram was made. We have not felt that disproportion between estimated age of fetus and duration of gestation was significant unless it amounted to a month or more, and in this case would not be willing to diagnose fetal death on the disproportion. The fetal skeletons were faint and we might have interpreted decalcification except for the large amount of fluid present, which could ac-

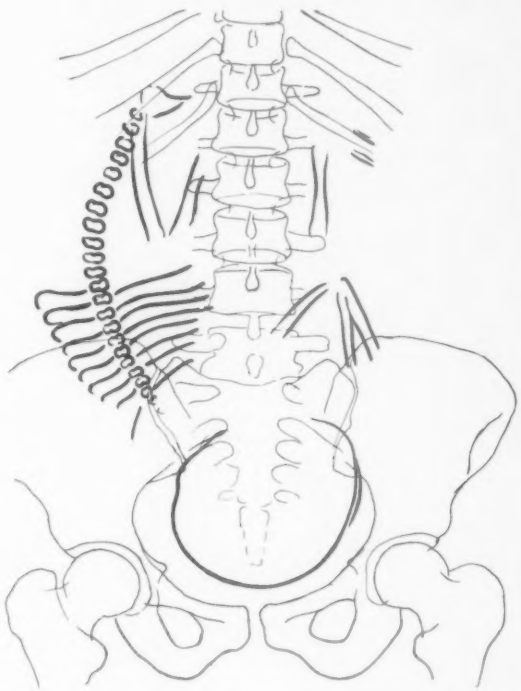


Fig. 3. Film tracing from Case XVI, subject in supine position. Live fetus at seven months, showing double contour of fetal skull where it is in contact with the left side of the maternal pelvis. Note also appearance of ribs, suggesting collapse of thorax. (Compare with Fig. 7.)

count for the faint shadow without the assumption of decalcification.

CASE XI (Unit #80585, X-ray #10806). J. S., aged twenty-four. Para 1; Wassermann negative. Onset of last menstruation, December 10, 1929. Predicted term, September 17, 1930.

August 7, 1930. Fetal heart tones heard.

August 11, 1930. Fetal heart tones not heard.

August 25, 1930. Fetal heart tones not heard.

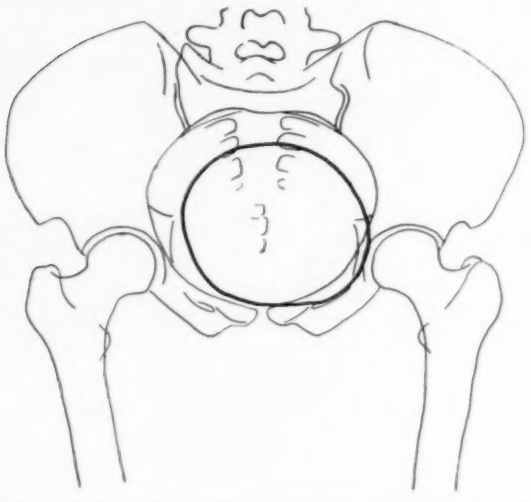


FIG. 4. Film tracing from Case XVI, subject in semi-recumbent position. The frontal suture, which in the supine film produced a double contour of the skull, is no longer confused with the margin of the skull and there is now no suggestion of overlapping of skull bones.

Patient has not felt fetal movement for six weeks.

August 25, 1930. Roentgen findings: A single fetus in cephalic presentation. Fetal skull not seen, almost certainly anencephalic and not a decalcified skull obscured by maternal pelvis. Question collapse of thoracic cage. No other criteria present.

October 2, 1930. Spontaneous delivery of a macerated anencephalic monster thought to be of five months' development.

CASE XII (Unit #83891, X-ray #13699). L. S., aged twenty-three. Para 1; weight 114; Wassermann negative. Onset of last menstruation, June 7, 1930. Predicted term, March 14, 1931.

February 16, 1931. Suspect breech presentation.

February 27, 1931. Polyhydramnios—monstrosity?

February 27, 1931. Roentgen findings: A single fetus in transverse presentation. Absence of head. Marked angulation at caudal end of spine. Question of collapse of thorax.

March 1, 1931. Spontaneous delivery of a dead anencephalic fetus with spina bifida.

CASE XIII (Unit #78538, X-ray #350). K. B., aged twenty-six. Para III; weight 138 lb; Wassermann negative. Onset of last menstruation, October 27, 1929. Predicted term, August 3, 1930.

January 8, 1930. Uterus of about three months' development.

January 8 to May 20, 1930. Examination every two weeks. Essentially negative.

May 9, 1930. Roentgen findings: Single fetus in cephalic presentation—age estimated from occipito-frontal diameter, seven and one-fourth months. No criteria of death present.

May 30, 1931. Breech extraction of a macerated fetus thought to be of about eight months development.

Note. There are several discrepancies in the case which are all cleared up if we assume that the menstrual history is in error by one month. Assuming that term should have been predicted for July 3 instead of August 3, the gestation would have been at seven and one-quarter months on May 9, which would have agreed exactly with the roentgen estimate of fetal age. Assuming further that the fetus was alive at the time the examination was made (and there is no note in the record to indicate that it was dead at that time), if the child continued to live for a few weeks it would have been about eight months old at the time of its death, shortly before breech extraction, May 30, 1931. The absence of decalcification or skull overlapping supports this view.

CASE XIV (Unit #38856, X-ray #17305). K. C., aged thirty. Para IV; weight 135 lb.; Wassermann negative (case of treated syphilis). Onset of last menstruation, January 19, 1931. Predicted term, October 26, 1931.

May 25, 1931. Active fetal movements.

September 14, 1931. Fetal heart tones normal.

September 21, 1931. There have been no fetal movements or fetal heart tones for the past week.

September 20, 1931. Roentgen findings:

Single fetus in cephalic presentation—age estimated from occipito-frontal diameter, seven and seven-eighths months. No overlapping of skull bones, angulation of spine or any other criteria of death.

October 5, 1931. Delivery of macerated fetus thought to be about thirty-seven weeks old. The state of maceration suggested that the fetus had been dead approximately twenty days.

Note. Estimating from the menstrual history, gestation was of seven and three-fourths months' duration on September 20, 1931, which coincides within three and one-half days with the roentgen estimate of the fetal age. Assuming this estimate to be correct, the fetus must have been alive or very recently dead at the time the roentgenogram was made. This agrees with the clinical history of normal fetal heart tones September 14, as well as with the guess on October 5 that the macerated fetus had been dead approximately twenty days.

ABSTRACTS OF 8 ILLUSTRATIVE CASES FROM THE GROUP OF 162 CASES IN WHICH THE FETUS WAS ALIVE

CASE XV (Unit #82688, X-ray #12575) (Fig. 2). N. A., aged thirty. Para 1; weight 233; Wassermann negative. Onset of last menstruation, January 4, 1930. Predicted term, November 11, 1930 (note discrepancy). No information as to fetal heart tones and other clinical findings.

December 20, 1930. Roentgen findings: Single fetus in cephalic presentation—occipito-frontal diameter shadow 15 cm.; less 20 per cent, 12 cm.; plus 1 cm. for overlapping, 13 cm. Age estimated "over term." Frank overlapping of cranial bones.

December 20, 1930. Patient had been in labor sixteen hours at the time the roentgen examination was made and continued in labor eleven hours afterwards, at the end of which time caesarian section was done. Measurements of the child's skull after delivery are recorded as follows: O.F., 12.5. Bi-P., 9.5. Bi-T., 8.5 Subo. Breg., 10. O.M., 14. Circumference—first 32, second 36.

Note. There are obvious discrepancies in the menstrual history but we feel that our roentgen estimate of a fetus well "over term" is borne out by the subsequent events connected with the delivery.

CASE XVI (Unit #47362, X-ray #18273) (Figs 3, 4 and 10). A. S., aged twenty-one. Para II; weight 105; Wassermann negative. Onset of last menstruation, March 5, 1931. Predicted term, December 12, 1931.

November 14, 1931. Fetal heart tones heard.

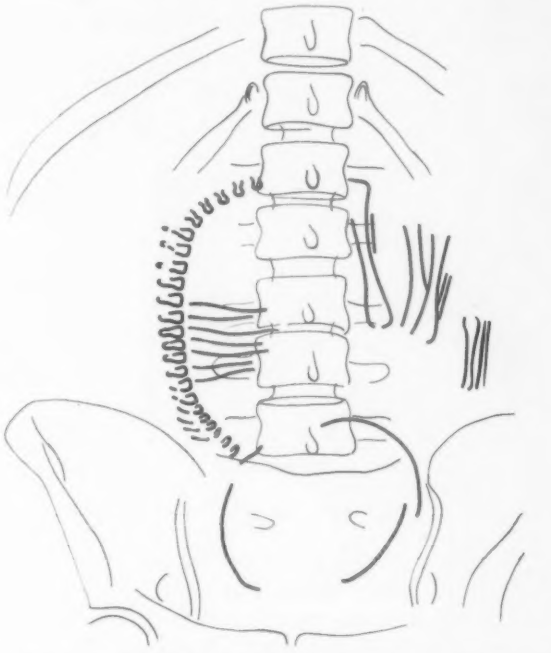


FIG. 5. Film tracing from Case II, subject in prone position. Dead fetus at term, showing angulation of caudal end of spine. Note also overlapping of skull bones. Decalcification of skeleton not illustrated in tracing.

November 14, 1931. Roentgen findings: Single fetus in cephalic presentation—age estimated from occipito-frontal diameter, seven and one-fourth months. Questionable overlapping of skull bones; also question thoracic collapse. The second film, after special positioning, shows absence of overlapping.

December 2, 1931. Spontaneous delivery of normal living child.

Note. Estimating from the menstrual history, duration of gestation was of seven and five-eighths months on November 14, so that the roentgen estimate of fetal age agrees with the estimated period of gestation within about ten days. Figure 3 illustrates the accidental double contour;

Figure 4, a normal skull as visualized in special position. Note appearance of thorax here as compared to that in Case VII, Figure 7. In that case the fetus was born

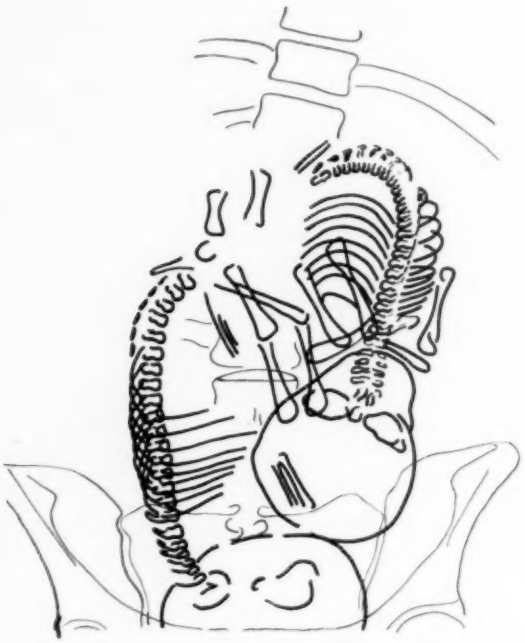


FIG. 6. Film tracing from Case XVII, subject in prone position. Live twins at eight and one-half months. The upper twin, which lies at the left side of the maternal abdomen, shows marked angulation of the caudal end of the spine, presumably due to crowding.

dead and the thoracic collapse was supposedly significant. Here it is an accidental finding. The patient was not in labor at the time the roentgen examination was made.

CASE XVII (Unit #77700, X-ray #323) (Fig. 6). H. M., aged twenty-eight. Para 1; weight 104; Wassermann negative. Onset of last menstruation, July 12, 1929. Predicted term, April 19, 1930.

March 10, 1930. Suspect polyhydramnios.

April 14, 1930. Suspect twins.

April 17, 1930. Roentgen findings: Two fetuses in cephalic presentation—skulls in oblique position—cannot measure occipito-frontal diameter. No overlapping of skull bones but marked caudal angulation of spine of the upper fetus.

April 18, 1931. Delivery of normal twins at term.

Note. The angulation of the spine appears to be due to crowding. We did not undertake to measure any of the other diameters; first, because we have had little experience with them but believe that in most cases they will, in the absence of steroscopic triangulation, be subject to much greater errors than the occipito-frontal diameter; second, because we assume that the Scammon and Calkins formula does not apply to twins.

CASE XVIII (Unit #40377, X-ray #15702) (Figs. 8 and 10). M. G., aged twenty. Para 1; Wassermann negative. Onset of last menstruation, September 29, 1930. Predicted term, July 6, 1931.

May, 1931. Fetal heart tones normal.

June 24, 1931. Roentgen findings: Single fetus in cephalic presentation. Age estimated from occipito-frontal diameter, nine months (see note). Frank overlapping of skull bones and angulation of spine. One extremity has moved during the roentgen examination—positive proof of the fact that the fetus is alive.

FIG. 7. Film tracing from Case VII, subject in prone position. Dead fetus of seven months' development showing what we interpret as the thoracic collapse described by Matthews but not illustrated in his publications. (See Fig. 3 for similar appearance in a live fetus.) The case also shows angulation of the dorsal spine.

June 25, 1931. Low forceps delivery of a normal living child.

Note. The overlapping of the skull bones is unquestionably due to labor which had been present for twenty-four hours at the time the roentgenogram was made. Age estimate made as follows:

O.F.D. shadow, less 20 per cent for distortion	11.4 cm.
Plus 1 cm. added to correct for the molding of labor (Scammon and Calkins)	1 cm.
Total	12.4 cm.

From the curve an occipito-frontal diameter of 12.4 cm. indicates a fetus of nine months' development.

CASE XIX (Unit #2752, X-ray #969) (Figs. 10A and B). W. L., aged twenty-nine. Onset of last menstruation not accurately known, approximately September, 1927.

March 6, 1928. Roentgen findings, subject prone. Very small fetus in breech presentation lying high up in maternal abdomen. Age estimated from occipito-frontal diameter, three and three-eighths months.

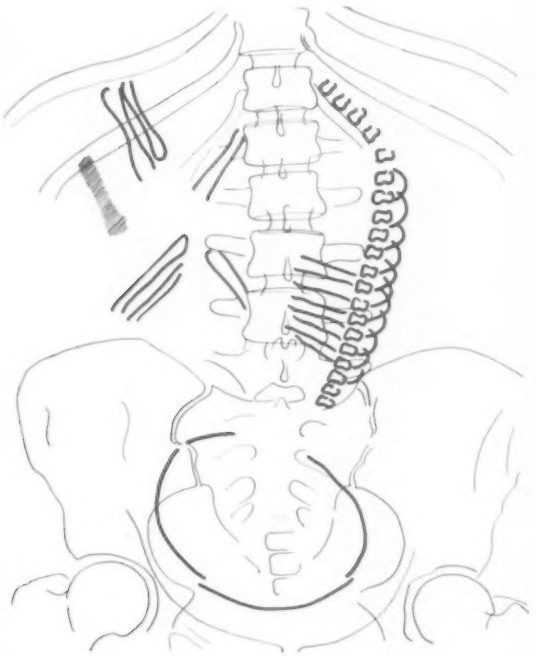


FIG. 8. Film tracing from Case XVIII, subject in supine position. Blurring of the shadow of one of the fetal extremities is positive evidence of life. Overlapping of skull bones and angulation of the caudal end of the spine are due to labor.

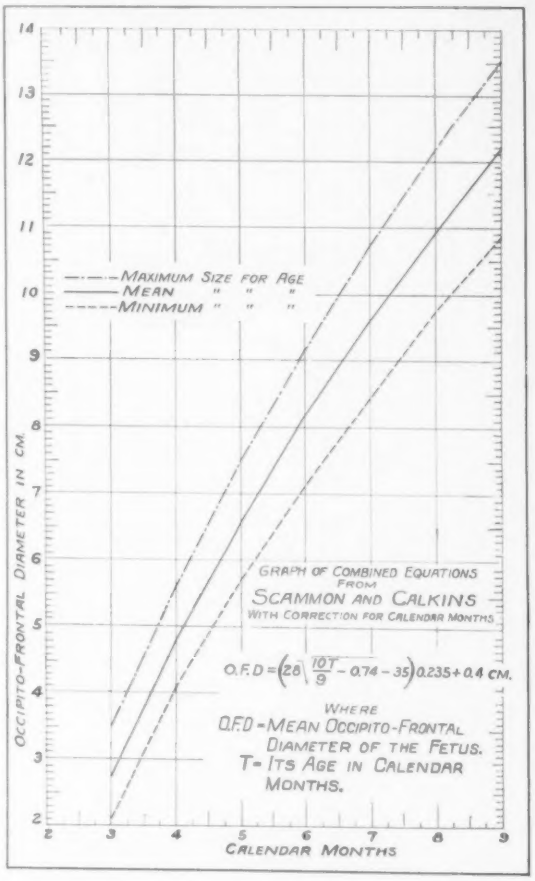

OCCIPITO-FRONTAL DIAMETER IN CM.
CALENDAR MONTHS
MAXIMUM SIZE FOR AGE
MEAN " " "
MINIMUM " " "
GRAPH OF COMBINED EQUATIONS FROM SCAMMON AND CALKINS WITH CORRECTION FOR CALENDAR MONTHS
O.F.D. = (28 √(10T/9) − 0.74 − 35) 0.235 + 0.4 CM.
WHERE
O.F.D. = MEAN OCCIPITO-FRONTAL DIAMETER OF THE FETUS.
T = ITS AGE IN CALENDAR MONTHS.

FIG. 9. In prone position, 36 inch target film distance roentgenograms where the sagittal plane of the fetal head appears to lie approximately parallel with the plane of the film, measure in centimeters the distance from the glabella to the inion and multiply this value by the correction factor, 0.80.

Assuming this product to be the occipito-frontal diameter of the fetus, lay it off on the vertical scale of the graph and at the intersection with the solid curve, read the probable age of the fetus in calendar months.

Broken curves show maximum and minimum variation from predicted age as observed by Scammon and Calkins in their study of fetal cadavers.

March 30, 1928. Fetus larger, lower and rotated into slightly different position. Age estimated from occipito-frontal diameter, three and three-fourths months.

August 24, 1928. Delivery outside of hospital of normal living child.

Note. Assuming spontaneous delivery August 24, the fetus was about three and

three-eighths months old at first examination and four and one-fourth months at the second examination.

CASE XX (Unit #47601, X-ray #19035) (Fig. 10). C. Y., aged twenty-eight. Para II; weight 125. Onset of last menstruation August 8, 1931. Predicted term, May 15, 1932.

December 18, 1931. Fetal heart tones not heard.

January 8, 1932. Uterine size suggests pregnancy at five months. Question of twins.

January 8, 1932. Roentgen findings: Subject prone. Single fetus in breech presentation—age estimated from occipito-frontal diameter, four and three-eighths months.

Note. Failure to hear fetal heart tones is not surprising at this age. No reason to doubt live fetus because patient felt fetal

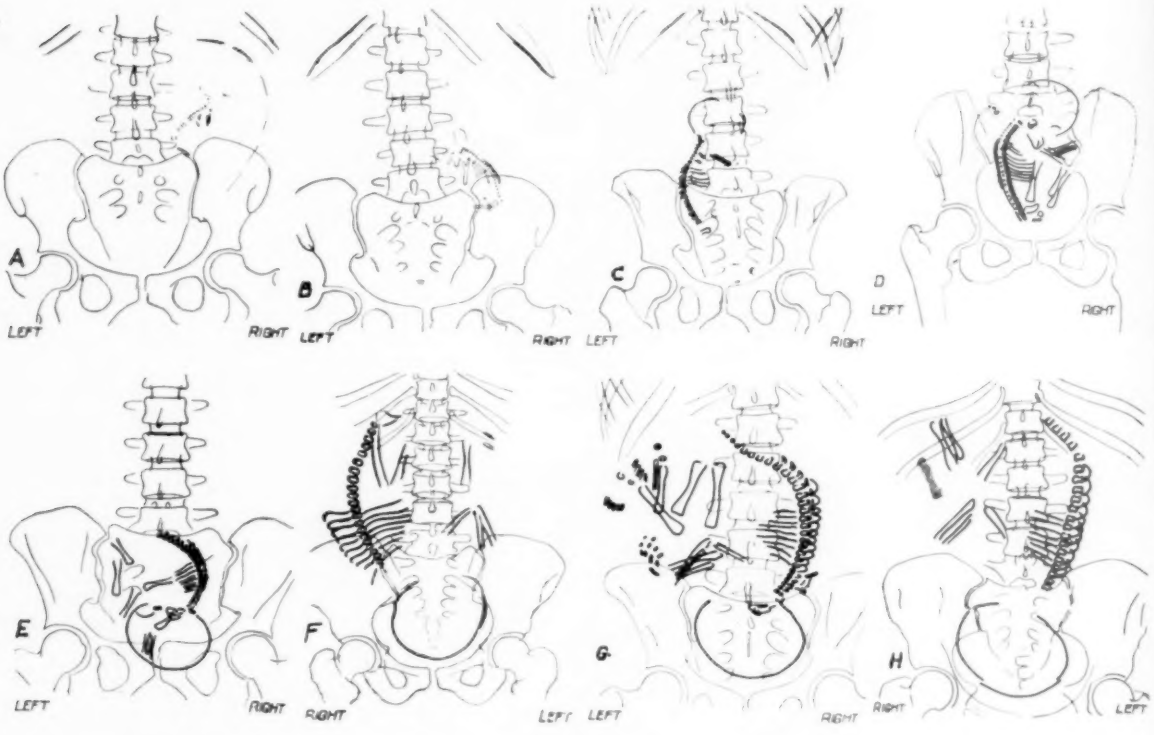


FIG. 10. Estimation of fetal age in utero by roentgenographic measurement of the skull. In 7 cases of live fetus, roentgen estimates of age correspond closely with age determined from menstrual history. In our Case D disproportion of 2 3/4 months indicates a fetus dead that period of time.

A. Case XIX. Live fetus, probably 3 3/8 months. Roentgen age and age estimated from delivery identical.

B. Case XIX. Same fetus at 4 1/4 months. Roentgen estimate now 3 3/4 months.

C. Case XX. Live fetus. Age estimated from menstrual history, 4 3/4 months. Roentgen age estimate, 4 3/8 months.

D. Case IV. Dead fetus of five months' development. Duration of gestation, 7 1/4 months. Roentgen estimate of age, 4 7/8 months. Fetus probably dead therefore for a period of 2 2/3 months at time of examination.

E. Case XXI. Live fetus. Roentgen estimate of age, 6 1/8 months. Age from menstrual history, 5 3/4 months.

F. Case XVI. Live fetus. Age estimated back from delivery, 7 5/8 months. Roentgen estimate of age, 7 1/4 months.

G. Case XXII. Live fetus. Age estimated back from delivery, 8 months. Roentgen estimate of age, 8 months.

H. Case XVIII. Live fetus at term, examination during labor. Roentgen estimate of age (corrected for overlapping), 9 months—that is, term.

movement at time examination was made. If patient's memory as to onset of last menstruation is correct, fetal age should be four and three-fourths months.

Case xxi (Unit #3004, X-ray #1029) (Fig. 10E). M. H., aged thirty-one. Para iv. Onset of last menstruation, September 14, 1927. Predicted term, June 21, 1928. March 12, 1928. Roentgen findings: Single fetus in cephalic presentation—age estimated from occipito-frontal diameter, six and one-eighth months.

June 1, 1928. Labor was induced, version and extraction done.

Note. Estimating from menstrual history gestation was of five and three-fourths months' duration on March 12.

Case xxii (Unit #83864, X-ray #13041) (Fig. 10G). G. K., aged twenty-three. Para i.

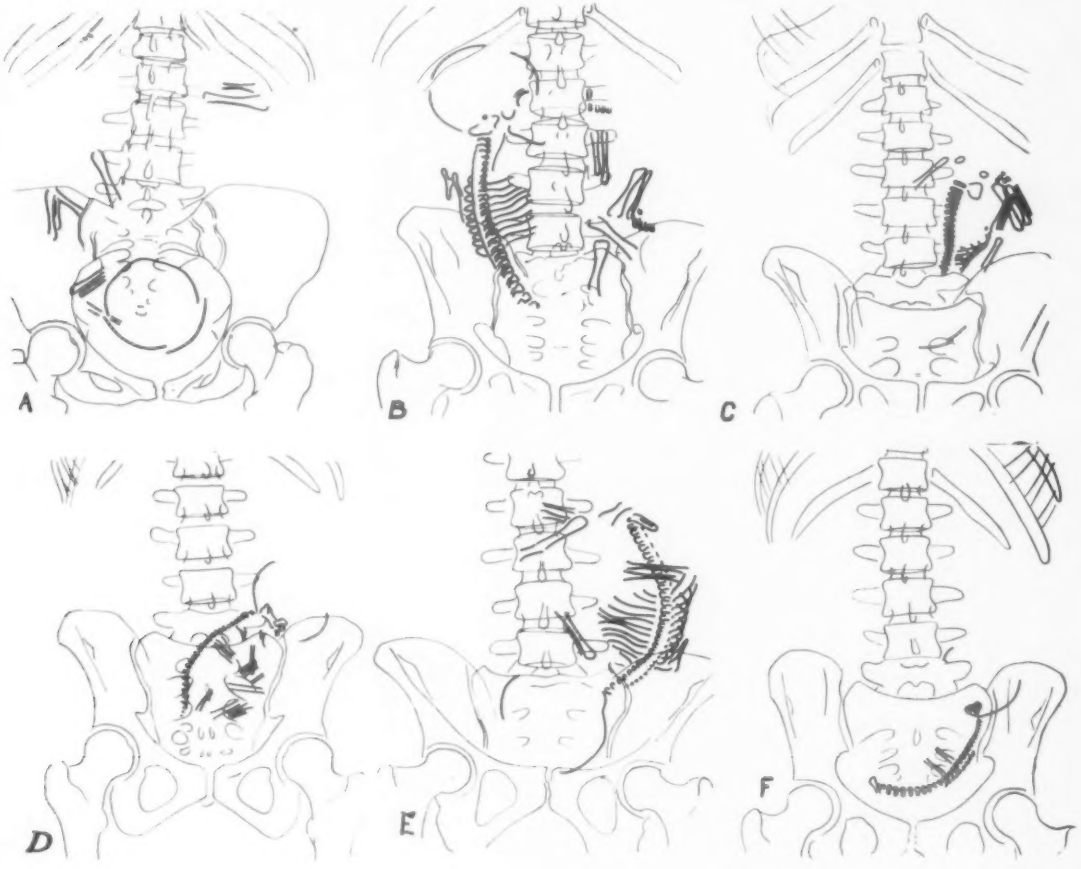


Fig. 11. Six cases diagnosed "dead fetus" because roentgen estimate of age is significantly less than the duration of gestation.

A. Case i. Duration of gestation, 9 months. Roentgen estimate of age, 6 months. Therefore fetus dead 3 months.

B. Case iii. Duration of gestation, 8 months. Roentgen estimate of age (corrected for hydrocephalus), 6 1/4 months. Therefore fetus dead 1 3/4 months.

C. Case v. Duration of gestation, 8 1/4 months. Roentgen estimate of age, 6 1/2 months (estimated from length of femur—skull not visualized). Therefore fetus dead 1 5/8 months.

D. Case vi. Duration of gestation, 6 5/8 months. Roentgen estimate of age, 5 3/8 months. Therefore fetus dead 1 1/4 months.

E. Case vii. Duration of gestation, 8 months. Roentgen estimate of age, 7 months. Therefore fetus dead 1 month.

F. Case ix. Duration of gestation, 7 3/4 months. Roentgen estimate of age, 5 1/2 months. Therefore fetus dead 2 1/4 months.

Onset of last menstruation, April 26, 1930. Predicted term, February 3, 1931.

January 2, 1931. Fetal heart tones heard.

January 20, 1931. Roentgen findings: Single fetus in cephalic presentation—age estimated from occipito-frontal diameter, eight months.

February 21, 1931. Delivery of normal living child thought to be at term.

Note. Estimating from delivery the age on January 20 *was* eight months as estimated by the roentgen ray. It seems reasonable to assume that the menstrual history is in error.

EVALUATION OF THE CRITERIA

Overlapping of Skull Bones. The 3 cases in which we have been able to demonstrate overlapping of the skull bones constitute 25 per cent of the 12 cases of dead fetus (two anencephalics excluded). All three were in cephalic presentation.

In Case I (Figs. 1A, 1B, 11A), where the fetus had been dead approximately three months, there can be little question as to the fact that overlapping was present and was the result of maceration rather than labor molding. On the other hand, the clinical diagnosis was well established before the roentgen examination was made and several other roentgen criteria were present.

In Case II (Fig. 5), the fetus had been dead not more than a week, was at term and well developed. Overlapping of skull bones was perfectly frank. If we can be certain that labor had not begun at the time the film was made, this appears to be a case of brain shrinkage occurring very early in maceration.

Skull visualization in Case V (Fig. 11C) is so poor that the diagnosis of overlapping is somewhat difficult to defend. We had trouble deciding whether to include this as a case of overlapping or to carry it with the group in which no statement could be made.

We are not prepared to condemn the positive value of the overlapping criterion on information from such a small number of cases but must point out that our figure for the incidence of overlapping in normal cases during labor is almost the same as that for death (25 per cent) and that, furthermore, we believe the roentgen appearance to be identical in the two conditions.

More than 7 per cent of normal cases not in labor showed pseudo-overlapping due to superimposed shadows of sutures or fontanelles that was most difficult to distinguish from genuine overlapping (Fig. 3). Re-examination using stereoscopic films in the semi-recumbent position frequently clears up such problems (Fig. 4) but when opinions must be rendered on a single non-stereoscopic film there are apt to be mistakes.

Absence of overlapping is by no means an assurance that the fetus is alive. We failed to find the sign in 75 per cent of 12 cases (2 anencephalics excluded). Assuming that as maceration progresses the brain does shrink and the skull bones do become overlapped, still there are at least three factors which might prevent the appearance of the criterion in a particular dead fetus:

(1) Tengbergen has reported 2 cases of hydrocephalic dead fetuses in which the skull bones were not overlapped and our Case III (Fig. 11B) is a third such instance. If, as some pathologists state, the fluid in the ventricular system of a hydrocephalic fetus continues to collect after death, it seems reasonable to suppose that this would offset the effect of brain shrinkage and prevent overlapping of the skull bones.

(2) Poor visualization due to faint shadow or to the overlying shadows of maternal pelvic bones, intestinal gas, etc., may make it impossible to state whether or not overlapping is present. Cases IV, VI, VII, VIII and IX illustrate this point. Re-examination with slightly different technique may occasionally help in such cases.

(3) Some time must elapse between the death of a fetus and shrinkage of its brain to the point where overlapping of the skull bones results. A fetal skull roentgenographed during this interim period (what-

ever its length may be) will fail to show overlapping in spite of the fact that the fetus is dead. It is our opinion, admittedly not well documented, that genuine death overlapping is a late phenomenon and that supposed cases of early appearance of the criterion, our own Case II (Fig. 5) included, are really instances of molding due to unrecognized, or at least unrecorded, labor or engagement of the head. We hazard the guess that if other cases of supposed overlapping occurring soon after death are restudied, it will be found that in no instance was the fetus in breech presentation and in no instance of much less than nine months' development.

In Cases X and XIII of our series, skull bone overlapping was not present, but the fetus had been dead only a very short time when the films were made.

Angulation of the Spine. This sign is even less dependable than skull bone overlapping. It is true that we have seen some degree of angulation in some part of the spine in 50 per cent of our 14 cases of dead fetus, whereas it was present in only 11.5 per cent of the 147 normal pregnancies examined before the onset of labor. Furthermore, its incidence in normal pregnancies becomes even lower after 6 cases of twins are excluded. On the other hand, when we are faced with a particular case showing angulation of the spine and must decide whether or not the fetus is dead, we have only the mathematical probabilities to guide us because the angulation occasionally seen in a live single fetus (Fig. 8) and more frequently in twins (Fig. 6) is in every respect identical with that of death.

Collapse of Thorax. Two of our cases show a somewhat peculiar arrangement of ribs and we have illustrated one of them by a film tracing (Fig. 7) with the idea that it may be an instance of the thoracic collapse that Matthews has described but not illustrated. Autopsy measurements of the chests of macerated and unmacerated fetal cadavers are not available but there seems to be a general impression that the thorax does collapse as maceration progresses. On the other hand, Browne[6] describes an expansion of the thorax occasionally seen in still-births.

Faint Shadow (Decalcification). The idea that the skeleton of a dead fetus undergoes partial decalcification in the process of maceration is by no means generally held by obstetricians and embryologists. In cases of missed abortion (in human subjects) before the fetal skeleton has acquired calcium, it appears to be established that total absorption of fetal tissue may occur, but we have not been able to find published instances where such absorption was known to have occurred in a skeleton that had once contained calcium. Arguing from the situation that obtains in non-vascularized fragments of a fractured hip and the sequestra of chronic osteomyelitis, one might assume that since the macerated fetus does not acquire a peripheral blood supply from the uterine vessels, the fetal bones, once they had acquired calcium, could not lose it. On the other hand, Bartelmez,[3] while by no means defending the theory of decalcification in maceration, points out that it is not entirely illogical to assume an ability of maternal tissue to absorb dead fetal bone by some cell or tissue reaction not dependent upon a definite vascularization. He doubts the likelihood of this and reminds us that grossly macerated syphilitic fetuses commonly show a skeletal system that appears normal to casual inspection and is rigid enough to be easily pulled loose from the macerated soft tissue. We are not sufficiently acquainted with the literature dealing with the absorption of dead fetuses in rats and other laboratory animals to know whether this ever takes place after calcification of the skeleton has occurred.* Bartelmez reminds us, however, that there might well be striking differences between the process of maceration in the human embryo where extrusion of a dead fetus is the rule and the situation in lower animals where absorption of a dead fetus

* In experiments by Long and Parkes[26a] the soft tissues of embryos of laboratory animals autolyzed a little over a week at 37°C., were completely destroyed while the skeletons remained intact.

commonly occurs. There is, of course, a very real possibility that "faint shadow" while really due to a lack of calcium in the fetal skeleton still depends upon faulty calcification or calcium depletion occurring during the life of the fetus as a feature of the conditions that caused its death rather than upon decalcification occurring after death. In cases of fetus compressus where one of a pair of twins dies early and the other goes to normal delivery, the fetal skeleton of the dead twin has been found to be quite normal in appearance, and, of course, in lithopedions the skeletal structure may persist for months or years (Adair[1a]).

This uncertainty as to the essential facts makes it precarious to discuss the roentgenographic interpretation of decalcification as a criterion of fetal death, and we have used instead the term "faint shadow" to describe the blurring and indistinctness encountered in 7, or 50 per cent, of our 14 dead fetus cases and not in any of the 162 live fetuses. The change is apparently a late one because it was present only in cases where the fetus had been dead for a month or more. As an isolated observation it is a dangerous criterion because of possible confusion with faint shadow caused by overpenetration, excess fluid and other technical factors. As supporting evidence, however, in cases showing disproportion, it is perhaps a helpful sign.

Disproportion. Obstetricians make routine use of the principle of disproportion when they estimate fetal age in terms of uterine size and consider the finding suggestive of death of the fetus if that size is definitely small for the supposed duration of gestation. Tengbergen and Henrotay, who described disproportion as a roentgen criterion, do not explain the means used to determine fetal age from roentgenograms but we assume that they used measurements of skull and trunk diameters rather than an estimate of the degree of ossification of epiphyseal centers because, as far as we know, work such as that of Adair and Scammon on the roentgen appearance of fetal epiphyses has all been done on laboratory material rather than on the fetus in utero. Three distinct problems are involved. The first of these is the relationship between measurements of the roentgenogram and actual skull, trunk or extremity dimensions of the fetus. The second has to do with the relationships between these dimensions and fetal age and the third is the estimation of the duration of gestation from menstrual history.

Thoms[51,52] and Walton[53,54] each using his own modification of the position method, have concluded that they were able to make reasonably good guesses of the size of a fetus. They use the principle expressed in the formula

$$O = X\frac{D-Y}{D}$$

where

O = True diameter of a flat object lying parallel with the roentgen film, its center on a perpendicular dropped from the target of the roentgen tube to the center of the film.

X = Diameter of its roentgen shadow.

D = Perpendicular distance from target of roentgen tube to surface of film.

Y = Perpendicular distance from center of object to surface of film.

X and D can be measured with any desired degree of accuracy but Y is determined solely by physical examination of the patient as she is positioned on the roentgen table just before the film is made. There is a further difficulty in the fact that fetal parts, particularly the skull, are not flat, and physical examination of the patient, together with inspection of the completed film, supplies only the roughest idea as to the angular relationship between object and film. There are many other publications on the subject but we are not prepared to discuss them at this time.

The second problem belongs properly to the field of anatomy and has received much attention from embryologists, as evidenced by the fact that embryonic material is

commonly classified on the basis of its over-all length in centimeters and that many "rules" have been enunciated for the estimation of age from this length. Haase's rule is perhaps the best known.*

Scammon and Calkins in 1923 published the equation:

$L = 28\sqrt{T - 0.74} - 35$ where

L = Crown-heel length of a fetus in cm.

T = Fetal age in lunar months.

This was followed in 1929[36] by their monograph which included measurements of the skull, trunk and extremities of hundreds of fetal cadavers in which crown-heel length was known. The tables demonstrate a rather wide normal variation of any dimension, such as the occipito-frontal diameter, in fetuses of supposedly the same age as estimated from crown-heel length. Furthermore, critics of the work have been concerned as to the dependability of correction factors used to compensate for artefacts produced by differences in preserving fluid, etc.

The third problem has to do with clinical obstetrics and embryological theory plus the inevitable factors of carelessness and vagueness involved in recording menstrual history.

The situation appeared hopeless from all three angles and we began to study our material for the disproportion criterion, with no expectation of success. The films were old, for the most part non-stereoscopic, and therefore not subject to examination by parallax methods of measurement. Even if the fetal cadaver were before us so that inaccuracies of roentgen measurements might be avoided, there was apparently considerable question as to the accuracy with which its age could be determined. The prediction of term by adding seven days to the date of onset of the last menstruation and counting forward nine calendar months from that date was considered reasonably accurate in the majority of cases but was at best an approximation occasionally subject to unavoidable errors of as much as a month and grossly misleading where the patient's history was given carelessly or with deliberate intent to deceive. In spite of these difficulties, we decided to make an attempt, however, and proceeded as follows:

Our roentgenograms had for the most part been made with a target-film distance of approximately 35 inches, the subject prone on a Potter-Bucky grid table. There was obviously great variation in the distances between the various parts of a particular fetus and the plane of the roentgen film, to say nothing of the difference between one case and another. Rough measurements and calculations on a few test subjects, however, indicated a mean distance from the center of the skull to the film of approximately 7 inches for all cases.* Substituting in the formula

$$O = X\frac{D - Y}{D}$$

we obtained

$$O = X\frac{35 - 7}{35} = \frac{4}{5}\ X.$$

This means that if our assumption of object-film distance is correct, the diameter of a skull shadow seen in the roentgenogram is 20 per cent larger than the diameter of the skull that cast the shadow.

Inspecting our roentgenograms we discarded those in which the fetal skull could not be visualized or in which there was obvious obliquity between the sagittal plane of the skull and the plane of the roentgenogram. In the remaining ones, the outline of the skull was sketched in with a wax pencil, frequently by the aid of a reading glass, points were located at approximately the glabella and the inion and the straight-line distance between these two was measured in centimeters. This value was multiplied by 0.80 on the assumption of 20 per cent distortion due to angulation of radiation, also by 0.75 and 0.85 so that we might later test the reasonableness of our guess. Subsequent testing against the

* Up to the fifth month, fetal length in cm. = (age in months)^2. After the fifth month, length in cm. = age in months $\times 5$.

* This value, independently arrived at, agrees well with the conclusions of Thoms, who estimates that the center of the fetal skull lies approximately 15 cm. from the film in most instances

graph indicated that 20 per cent was a better guess than either 15 or 25 per cent.

In no case was it really possible to make out glabella or inion as definite landmarks but, on the other hand, a general localization was quite easy and it was obvious that a shift of the points a few millimeters up or down along the curvature of the skull would not alter the length of the diameter materially.

In accordance with findings from the laboratory of Scammon and Calkins we added 1 cm. to the diameters of skulls where overlapping was present due either to maceration or labor, this addition being done, of course, after the distortion factor had been applied to the original film measurement.

Five cases (Cases IV, VI, VII, VIII and IX) presented rather poor visualization of the skull and it had been felt that perhaps this fact explained failure to recognize overlapping of the skull bones. In all of these, however, we were able to make out enough of the skull outline to permit a measurement of the occipito-frontal diameter. In Case V, on the contrary, where we could make out overlapping at the fronto-parietal suture, the occiput was not visualized at all and so the occipito-frontal diameter could not be measured. One of the femora, however, seemed to lie parallel with the film, and though we recognized the uncertainty of this assumption and the additional fallacy of interpreting the length of the calcified part of the shaft of a fetal bone in terms of measurements made from the knee to the great trochanter in fetal cadavers, we did attempt the measurement and by means of tables from the Scammon and Calkins monograph were able to make a guess at the age. The method should be particularly useful in anencephalics but will seldom be applicable without the aid of parallax methods of measurement.[21] This is due to the fact that distortion produced by lack of parallelism between the planes of object and film is much more important in the case of a rod-like structure such as a femur than it is in the fetal skull which is frequently almost a sphere. We could not make the measurements in our two dead anencephalics.

Being now in possession of more or less accurate measurements of the occipito-frontal diameters of the skulls in a considerable number of cases, we sought for a convenient means of calculating age from this measurement.

Converting Scammon and Calkins' formula for the relationship between the occipito-frontal diameter and crown-heel length to read in centimeters instead of millimeters

$$O.F.D.\text{ in mm.} = C.H.\text{ in mm.} \times 0.235 + 4.0\text{ mm.}$$

and combining it with the 1923 formula for fetal age

$$L = 28\sqrt{T - 0.74} - 35$$

we obtained an expression of *O.F.D.* in lunar months. A calendar month is approximately 10/9 of a lunar month, so substituting $10T/9$ for T, the equation was written

$$O.F.D. = \left(28\sqrt{\frac{10T}{9} - 0.74} - 35\right)0.235 + 0.4\text{ cm.}$$

where

O.F.D. = Occipito-frontal diameter in cm.
T = Fetal age in calendar months.

This equation was solved for the seven months from three to nine and the solutions expressed in a graph (Fig. 9). The broken curves for range above and below predicted term are not calculated but were sketched in by locating on the graph certain of the observed variations recorded in the Scammon and Calkins Table 27.

The degree of coincidence between roentgen and menstrual estimates of ages in the 7 cases of living fetus that have been illustrated in Figure 10 is typical of the results in the other normals studied and while we do not consider any adaptation of the position method of fetometry really suitable for the estimation of fetal age, it is surprising to find that our present rough

methods allow guesses correct within a plus or minus range of two weeks. Because so many approximations are involved, we have not considered as significant a negative variation of less than twice the maximum error encountered in the normal cases—that is, we have not diagnosed dead fetus on the basis of disproportion unless the roentgen estimate of age was at least a month less than the duration of gestation as estimated from the menstrual history.

On this basis 7, or 50 per cent, of the dead cases show disproportion (Figs. 11 and 10D), the amount ranging from one month in Case VII to three months in Case 1. In 4 of the cases there is clinical confirmation of our guess as to the length of period during which the fetus has been dead and in the other 3 that part of the clinical record conflicting with our estimate is itself open to question.

While we have stressed the inaccuracies of fetometry by position methods and have alluded to the possibilities of parallax measurements, it must not be assumed that methods useful in the measurement of the maternal pelvis[21] can be applied directly to measurement of fetal parts. As a matter of fact, there are many difficulties to be overcome. With roentgen machines, films and screens available at present, the exposure time is of the order of five seconds for a satisfactory pelvic film late in pregnancy and the placing of the second film, recocking of the grid and the beginning of the second exposure occupy fifteen or twenty seconds or even more. These factors make it impossible for the patient to hold her breath throughout the making of a pair of stereoscopic films. It is difficult to be sure that the second inspiration will be of exactly the same depth as the first one. It is hard to prevent maternal movement between the making of the films and, of course, there is no means whatever of suppressing fetal movement during this period. In a few cases studied by us the fetus has remained quiet and parallax measurements in utero check reasonably well with measurements on the infant after delivery, but in other cases there has been obvious movement of fetal parts which leads to highly erroneous calculations of fetal size. Unquestionably means will be found to overcome part or all of these difficulties, but at the moment rough calculations from some type of "position method" appear to be the best means available for measuring the size of the fetus in utero.

One of the cases (Case IV, Fig. 10D) illustrates the great possibilities of roentgen measurements as a means of diagnosing fetal death. At two examinations, a week apart, skull measurements were identical. In this case the fetus was dead and so the skull should not have changed its size, but in view of the numerous factors that might have produced a fictitious change in measurements obtained by the position method, it is surprising that the two measurements coincided.

When and if roentgenographic fetometry acquires exactness, it may be possible to make a confident statement as to the life or death of a fetus at any time after the fourth month, sometimes earlier, on the unsupported evidence from two roentgen examinations a week or even less apart. A diagnosis of this sort available at a time when the failure to hear fetal heart tones is not significant, a diagnosis not requiring the support of a possibly erroneous menstrual history, would probably be of genuine value to obstetricians.

CONCLUSIONS

Based on a study of roentgenograms of 176 cases of pregnancy in which the fetal age at the time of roentgen examination ranged from three and three-eighths months to over term and in 14 of which the fetus was dead, the following conclusions have been drawn:

1. Roentgenographic demonstration of overlapping of the skull bones of a fetus in utero is fairly reliable evidence that the fetus is dead, provided the patient is not in labor and that care has been taken to exclude pseudo-overlapping due to the overlying images of sutures and fontanelles.

2. Absence of overlapping means little. Conclusive evidence is lacking as to the exact relationship between the date of fetal death and the development of the sign but all agree that some time must elapse. A faint fetal shadow may mask overlapping; hydrocephalus may prevent its development.

3. Spinal angulation and thoracic collapse appear to be of doubtful value as criteria of fetal death.

4. It is dangerous to diagnose decalcification in every instance of a faint or blurred fetal shadow because early in pregnancy the appearance may be due to a failure to calcify rather than a loss of calcium previously present and even in well-calcified skeletons, excessive amniotic fluid, respiratory movement and many technical factors can produce the same appearance. Furthermore, quantitative information is lacking as to the calcium content of the human fetus, either macerated or normal, and some embryologists and clinicians insist that no decalcification occurs in maceration.

5. Anthropometric data published by Scammon and Calkins allow a reasonably accurate opinion as to the age of a fetus if its occipito-frontal diameter is known. Even with very coarse roentgenographic measurements of this diameter, roentgen estimates of fetal age have agreed surprisingly well with the actual age (as estimated from menstrual or delivery dates) in a considerable number of cases. Disproportion between ages thus calculated and the supposed duration of gestation constitutes a valuable criterion of fetal death and accurate fetometry by stereoroentgenographic methods ought to improve the validity of the diagnosis.

6. Absence of any one or all of the criteria does not exclude the possibility that a fetus is dead because they all depend upon the degree of maceration. It seems worth while, therefore, to point out that the roentgenographic diagnosis of movement of a fetal part occurring during the roentgen examination constitutes conclusive evidence of fetal life.

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HEMANGIOMA OF THE VERTEBRA

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HEMANGIOMA of the vertebra from a clinical aspect is a rare disease. There have been only 13 clinical cases reported. The following one makes a total of 14 cases:

History. Miss E. B., Swedish, aged twenty-five, maid, entered the Ravenswood Hospital March 24, 1931. Her family history was irrelevant. She had never been ill till 1924 when she began to have pain and fatigue in the region of the lumbar spine after working hard. The pain and fatigue gradually increased and within a year after the onset extended the entire length of the spine. Both would last for weeks uninterruptedly and then would disappear for periods as long as three months. At times the pain would be quite sharp. In 1926 she developed pain in the abdomen, especially on the right side and in the epigastrium, which seemed at times to be associated with the pain in the back. The abdominal pain often occurred one to two hours after meals and was relieved by taking food. This pain was never severe enough to cause her to go to bed or to stop work and it was never accompanied by fever. At that time she often vomited immediately after meals and the vomiting continued intermittently till the time of the present examination. In 1928 she was under the care of another physician who diagnosed her ailment as appendicitis and removed her appendix. For a few months after the appendectomy the pain in the abdomen seemed partly relieved.

Her appetite was good. Her weight was 140 lb. (63.5 kg.); her greatest weight was in 1925 when she weighed 165 lb. (75 kg.). She never had any paralysis or incontinence of urine or feces.

Examination. The patient was fairly well nourished, with apparently some loss in weight and was 5 ft. 7 in. in height. The head, neck, and chest were negative. There was an area of tenderness in the epigastrium just below the xiphoid process. The spine was tender on percussion over the first lumbar vertebra. The extremities were negative. The deep reflexes were normal. Pain, temperature, touch, and kinesthetic senses were normal. The Babinski, Oppenheim, Gordon, and Romberg tests were negative.

Gastric analysis one hour after an Ewald meal showed a free acidity of 19 and combined of 8. The guaiac blood test of the stomach contents was negative. The stomach contents were 70 c.c. one hour after the Ewald meal. Urine and blood examinations (including Kahn and Wassermann blood tests) were negative.

Roentgenographic examination made by Dr. H. E. Potter showed a gastric ulcer. Roentgenograms of the first lumbar vertebra (Figs. 1 and 2) show a definite unusual characteristic appearance. Practically the entire body of this vertebra was affected. There were heavy lines of increased density running the entire length of the vertebra, in cephalad-caudad direction. They were slightly wavy or spiral, measured as much as 2 mm. in lateral thickness, and appeared to have more calcium in them than the normal vertebrae. They were present in the anteroposterior and lateral views. There were approximately eleven of these lines in the lateral view and approximately nine in the anteroposterior view. Between these dense lines and parallel to them were areas of approximately the same width, with increased bone penetration, or bone absorption. A few very narrow opaque lines ran at nearly right angles from the vertical lines, apparently connecting the vertical ones. The height and the width of the vertebra were normal and the bony arches and processes were not involved. The intervertebral discs above and below the first lumbar vertebra appeared normal.

Diagnosis. A diagnosis of probable hemangioma of the first lumbar vertebra was made. There was discussion regarding the diagnosis among some of the consultants who examined the roentgenograms, but Dr. Percival Bailey, who reported Case 12 below, stated that in his opinion the diagnosis of hemangioma was correct.

Treatment. The patient was placed on the routine Sippy management for the gastric ulcer. The hemangioma of the vertebra was treated with radium under the supervision of Dr. W. L. Brown. On April 2, 55 mg-hr. of radium was applied over the first lumbar vertebra with 0.8 mm. of gold and 0.8

mm. of rubber screening; April 24, 50 mg-hr. with 0.5 mm. of silver and 1.0 mm. of brass screening at 15 mm. distance, and on May 29, June 26, and July 31, respectively, 1,150 mg-hr. with 0.8 mm. of gold screening at 2.5 cm. distance was applied. No further radium treatment will be given for three months, after which roentgenograms are to be taken to check the results of the radium therapy. The pains in the abdomen entirely disappeared within two months and the pain and weakness of the back ceased within four months (July 31) after the first application of radium.

Fig. 1

There have been only 13 cases reported, as noted above, besides the case here reported, showing symptoms of hemangioma of the vertebra and they are as follows:

Case 1.—Gerhard.[8,15] 1887. A baker, aged seventeen, in the course of three weeks had marked weakness of the legs. Seven months later, was unable to walk. Had no pains but there was loss of sensibility in the legs. Had no spinal deformity. Died after six years from erysipelas. Necropsy revealed a hemangioma of the 5th and 6th thoracic vertebrae and tumorous formation pressing the cord.

Case 2.—Deetz.[3] 1901. Female, aged forty-two. Died from compression myelitis. Also had a hemangioma of the liver. Ante-mortem diagnosis was sarcoma of the spinal column.

Fig. 2

Case 3.—Muthmann.[15,17] 1903. Female, aged sixty-one. Had sciatica since the age of forty-five. The sciatica improved for years, but then became worse and was followed by weakness in the legs. She had a dorsal kyphosis and the spinal column was painful to percussion in the region of the kyphosis. The patient died thirteen months after the onset with pyelonephritis, myocarditis, and decubitus. Clinical diagnosis: spondylitis. Necropsy showed a

cavernous hemangioma of the 6th thoracic vertebra and the 6th intervertebral disc, with cord pressure.

CASE 4.—Ribbert.[23] 1912. Young girl. Died from compression myelitis. The hemangioma formed a prominence on the side of the vertebra. Also had hemangioma of the liver.

CASE 5.—Trommer.[29] 1919. Female, weaver, aged seventeen. Had spastic paraplegia three weeks after the onset. Had pains late. There was pain on pressure over the 6th thoracic vertebra. Clinical diagnosis tumor of spinal column. Died after two years with flexion contractures and decubitus. At necropsy the 5th thoracic vertebra was broader than normal (the process extended into the costal neck) and contained a hemangioma which pressed on the spinal cord.

CASE 6.—Gold.[10] 1926. Miner, aged twenty-three, ill for five years, with weakness in legs, and subsequently developed spastic paraplegia. Patient had scoliosis but no gibbus. There was tenderness over the 7th and 8th thoracic vertebrae. Roentgenogram showed decalcification with spongious lamellae remaining. The height of the 7th and 8th vertebrae was lessened and the adjoining intervertebral discs were thickened. Preoperative diagnosis: spondylitis. Laminectomy was performed and the patient died from hemorrhage two hours after the operation. At necropsy a cavernous hemangioma was found in the 1st, 2d, 6th, and 7th thoracic vertebrae (roentgenogram did not show any abnormality in the 1st and 2d). Roentgenograms of the removed vertebrae showed the vertebral arches and articular processes to be involved.

CASE 7.—Perman.[20] 1926. Female, aged twenty-seven. Weakness in the knees began in 1920. She developed a spastic, ataxic gait and increased patellar reflexes. Diagnosis: unlocalized spinal tumor. Laminectomy was performed April, 1923, at which the dura pulsated and the 8th thoracic vertebra compressed the cord. Bleeding was controlled by wax, but a blood transfusion was necessary. The patient recovered. Roentgenograms taken in 1922 were considered negative but those taken in May, 1923 (one month after operation), showed thinning of the 8th thoracic vertebra and both transverse processes, but the intervertebral discs were normal.

CASE 8.—Guillain, Decourt, and Bertrand.[11] 1928. Male, aged eighteen. Symptoms began in 1925 with pain in the feet. Paraplegia soon developed and was complete in three weeks. There was a long dorsal scoliosis but no angular deformity. There was no tenderness over the vertebrae. Roentgenograms of the 7th, 8th, and 9th thoracic vertebrae showed the appearance of being blown up and the intervertebral discs were smaller than normal. Diagnosis: medullary compression. Laminectomy was performed in 1926 and the patient died from hemorrhage in a few hours.

CASE 9.—Globus and Doshay.[9] 1929. Female, aged thirteen. The patient developed weakness and stiffness of the legs one week after a fall. Later there appeared incontinence of the bladder and rectum. One year after the onset, spastic paraplegia, absent abdominal reflexes, bilateral ankle clonus and Babinski sign, and sensory loss below the 12th thoracic vertebra developed. Laminectomy was performed and the patient died following a severe hemorrhage from an aneurysmal vessel. Necropsy showed a hemangioma of the 8th thoracic vertebra.

CASE 10.—Ewing.[5] 1928. The patient developed a slowly progressive paraplegia due to a cavernous hemangioma of the thoracic vertebra. A collapse of the vertebra occurred with protruding tumor which compressed the cord. No operation was done.

CASE 11.—Makrycostas.[16] 1929. Female, aged seventy-five. The patient had pulmonary tuberculosis. An ante-mortem diagnosis of caries of the 5th lumbar vertebra and lobular pneumonia was made. No definite symptoms were mentioned. At necropsy hemangioma of the 3d lumbar vertebra was found.

CASE 12.—Bailey and Bucy,[1] and Bucy and Capp.[2] 1929. Female, aged sixty-two. Fell ten months before examination but recovered from this in two weeks. She had no further symptoms for five and a half months, when she had difficulty in walking. Seven months after the fall she developed a tight sensation in the abdomen. Later constipation, incontinence of urine, and weakness and loss of the sense of the lower extremities developed. Tactile hypesthesia developed in the abdomen, and hyperthermoesthesia and hyperalgesia above this. Signs of cord compression were also present. Roentgenograms of the 3d, 5th, and 6th thoracic vertebrae showed striations, areas of increased bone density, and absorption in the bodies and arches. The pedicles of the 5th and 6th were broadened. Diagnosis: probable metastatic tumor of the spine with compression myelitis. Laminectomy was performed November, 1928. The patient bled freely; the laminae of the 6th thoracic vertebrae were removed and the cord compression was relieved. Microscopically a cavernous hemangioma was found. Roentgen irradiation was later given with complete recovery.

CASE 13.—Ramage and Nattrass.[22] 1930. Male, aged fifty-one. Began early in 1929 with progressive weakness of the legs and gradual occurrence of numbness of the feet. Vibration sense was absent in the shins. Two months later ataxia and spasticity began. Abdominal reflexes were absent below the umbilicus and positive Babinski sign developed. Roentgenogram showed narrowing of the 8th dorsal vertebra on the right and on the front. The posterior border was indistinct and the pedicles were broadened. The trabeculae were thickened. Roentgen therapy was instituted. There was marked improvement eight months later and the vertical trabeculae became more evident.

There have been 393 cases with hemangioma of the vertebra found at necropsy, which showed no clinical symptoms, and they have been reported by nine different authors, as follows: Virchow[30] in 1863 described the first case on record. His patient was an old woman and a hemangioma of the liver was also found. Saltykow[24] in 1909, Fibiger[6] in 1912, and Pentmann[19] in 1915, each reported a case. Makrycostas[16] in 1927 found 41 hemangiomas of the vertebral column in 12 bodies, Schmorl[26] in 1927 found 115 in 1,142 bodies, or an incidence of 10.1 per cent, Töpfer[28] in 1928 found 257 in 2,154 bodies, or an incidence of 11.93 per cent, and Putschar[21] in 1929 found 4 in 56 vertebrae, or an incidence of 6 per cent. Eigler[4] in 1930 described one case associated with hemangioma of the liver, skull, skin, and lymph glands. Putschar searched in 25 children's bodies and found none, and Schmorl also searched in children's bodies with similar results.

The great majority of the patients have been adults. The youngest one reported whose age was definitely stated was aged one year and the oldest ninety. Females predominate in the ratio of 1.5 to 1.2 per cent in 265 cases. The majority of the cases reported have a definite origin in the marrow, but Ewing stated that a true cavernous angioma may arise from the periosteum. Töpfer suggests that hemangioma may be an embryonic proliferation.

Johnson[14] describes hemangiomas as being of the capillary, arterial, venous, and cavernous types. Kaufmann[15] divides hemangiomas into the cavernous and telangiectatic types and states that the cavernous type is most common. Hultén and Lovén[13] report a case of hemangioma associated with chondromata, both in bones and soft tissue. Hanson[12] demonstrated that two neighboring vertebrae may receive arteries from a common branch artery. This fact may explain why two adjacent vertebrae are sometimes affected by the hemangioma. He demonstrated by roentgenogram a bony defect or horizontal "splits" in the vertebral bodies which disappear during the second year of life but reappear again in old age. It is at the regions of the bony defect that the arteries and veins enter the vertebral body. Geist[7] states that there are also veins entering at the posterior part of the vertebral body. According to Sashin[25] and Schmorl the intervertebral discs normally have no blood vessels. This, perhaps, explains why the discs are so rarely involved in the hemangioma. In some of the cases the discs were involved; in Gold's case the adjoining discs were thickened but in the case of Guillain et al they were smaller than normal. Some hemangiomas have a capsule, according to Shaw,[27] and some have not.

The location in all cases has been in the thoracic or lumbar spine, and the lower thoracic spine is more often involved than the upper. The hemangiomata, as described, varied greatly in size; some were as small as a pepper seed and others completely involved one or more vertebrae.

Muthmann in 1903 gave the first complete histological description. Histologically, the cases have been described as having round, oval, square, thick or thin bony trabeculae with evident porosis. Töpfer states that the trabeculae may be 0.5 mm. thick and Putschar states they may be 1 mm. thick in the region of the hemangioma. The blood vessels were close together or widely separated, were large or small, and usually had a very thin wall, often of a single layer of epithelium. Ewing states that the walls of hemangiomas exhibit the structure of venules or less often of arterioles. Some had no limiting membrane and received vessels from the periphery. Osteoblasts and new bone formation are sometimes present.

The majority of the hemangiomas of the vertebrae described, as noted above, give no symptoms. Shaw stated that some hemangiomata may disappear spontaneously. The outstanding symptoms of the clinical cases were a progressive weakness of the lower limbs, with or without pain, passing to a paraplegia. All had a compression myelitis with perhaps one exception, in

which case a diagnosis of Pott's disease was made. Only one had kyphosis and one a protruding tumor.

Bucy and Capp[2] attempted to establish the disease process, hemangioma of the bone, as a roentgenological entity. Johnson states that the roentgenogram of calcifying hemangioma of soft tissue gives definite but not conclusive evidence as a diagnostic aid. Globus and Doshay doubt the value of roentgenography in diagnosis. Makrycostas in 1927 showed roentgenograms of his cases and thought it possible, as did Putschar and Gold, to arrive at a diagnosis by this means. Makrycostas described the vertical lines and atrophy and hypertrophy of the bony trabeculae seen in roentgenograms taken at necropsy, and uses the term "hypertrophic-atrophie" to describe his cases. Gold showed that the roentgenographic appearance corresponds very well to the active pathological condition. At necropsy Gold found hemangiomata in the 1st and 2d thoracic spine that did not show in the roentgenogram, thereby demonstrating that not all of them can be diagnosed by this method. Roentgenograms of Perman's case seven years before operation were negative. In contrast, roentgenograms taken six months before operation had definite changes but the diagnosis was missed, and those taken twenty days after operation showed thinning of the vertebra. Roentgenograms in the case of Guillain's were similar to Perman's and showed a "blown up" appearance of the vertebral body (the lateral surface of the vertebra was convex instead of concave), and thinning of the intervertebral discs. Bailey and Bucy state that the characteristic roentgenogram is pathognomonic of angioma of the vertebra. The case of Ramage and Nattrass is the only case reported previously that was diagnosed before operation or necropsy. This is perhaps true because no two clinical cases have been seen by the same person, so that when roentgenograms are examined, the unfamiliar appearance is not recognized.

The cases must be differentiated from tuberculosis, giant-cell tumor, sarcoma, osteoporosis, lues, myeloma, tumor metastasis, Kümmell's disease, osteoma, intervertebral disc nodes, osteomalacia, and gout. Tuberculosis usually causes a destruction of bone and is not associated with the vertical lines of increased density alternating with parallel lines of rarefaction. Giant-cell tumor, according to Bucy and Capp, usually expands the cortex with no new bone formation, while hemangiomas erode the cortex. Sarcoma breaks through the periosteum and hemangioma usually does not. Osteoporosis (includes osteitis deformans of Paget and osteitis fibrosa of von Recklinghausen in the classification of Schmorl), according to Schmorl, has rather early in its course, a very fine trabeculation in the center of the vertebra and very thick trabeculae at the periphery. Late, the whole vertebra has a very fine porosis. Lues is associated with a positive Wassermann reaction. Myeloma often breaks through the cortical region and is often quite painful, while hemangioma is usually not painful. Tumor metastasis may cause destruction or new formation of bone and is associated with the original tumor. Kümmell's disease is thought often to follow an infraction or fracture of the spine, has a lack of callus in roentgenogram, and is associated with a gibbus. The type of osteoma producing exostosis arises from the surface of the bone, according to Kaufmann. According to Schmorl and Geist, intervertebral disc nodes show a decrease in bone density in the roentgenogram extending from the intervertebral discs into the vertebral body. Only one case has been described in which the nodes were associated with a hemangioma. Osteomalacia is associated with a generalized ballooning of the discs. Gout is associated with changes in the urine.

The prognosis of the cases showing symptoms is bad. The majority of patients become bed-ridden and die of intercurrent infection. Gerhardt's case lived six years after the onset. The patients of Globus

and Doshay, Gold, and Guillain, Decourt, and Bertrand were treated by laminectomy but died soon after operation from shock and hemorrhage, while those of Perman and Bailey, Bucy, and Capp treated similarly recovered (60 per cent mortality). The patients of Perman, and Bailey and Bucy received roentgen therapy following operation, and Ramage and Nattrass treated their patient exclusively with roentgen therapy. None of them received radium therapy. The case here reported was treated with radium. Shaw states that it may require years of radium treatment of a hemangioma for complete recovery. Nielsen treated 784 patients with hemangioma from 1913 to 1926 with radium, and obtained good results in 90 per cent, fair results in 7 per cent, and had a failure in 3 per cent. He believes that radium is more certain to produce results and easier to apply to a given area than roentgen therapy. Perman suggests that Albee's bone graft operation might be tried.

SUMMARY

1. A review is made of all clinical cases of hemangioma of the vertebra previously reported.

2. The second case ever diagnosed before operation or necropsy is reported here.

3. Radium treatment was used with improvement.

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A METHOD OF MORE CLEARLY VISUALIZING LESIONS OF THE SIGMOID*

By WILLIAM H. STEWART, M.D., *and* H. EARL ILLICK, M.D.
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CANCER of the colon and especially of the sigmoid is a much more frequent lesion than is generally supposed and deserves more attention and consideration from the diagnostician as well as the roentgenologist. Too often it is an accidental finding during a routine examination and far too frequently it is overlooked even when present. We have all had the experience of re-examining cases at a later date only to find advanced pathology which had been missed on the first examination. The literature is full of the experiences of experts who admit failure in a large percentage of cases to demonstrate cancer of the colon until obstruction of considerable degree was present. The situation is a challenge to the roentgenologist to perfect his technique to the greatest possible degree in attempting to clearly visualize even early lesions so that mistakes may be few.

FIG. 1. The patient is retaining about one pint of a barium enema and has been turned with the right side upwards so that the body is at about a 45° angle, or in the most favorable position under the roentgenoscopic screen to visualize the sigmoid. A sandbag is placed beneath the right shoulder for additional comfort. The cassette is placed beneath the screen. The setting of the machine is changed for roentgenography and exposure of the film will give a permanent record of the outline of the sigmoid.

Cancer of the colon is insidious in onset and unless this possibility is ever before the physician so that his search may be thorough, early lesions will almost certainly be misinterpreted. The disease progresses slowly and the prognosis might be excellent if removal or treatment of early involvements were possible. Surgery is generally performed to relieve a completely obstructive lesion in which there is advanced metastatic involvement at the time of operation and the prognosis is necessarily hopeless. This situation must be changed and such lesions be diagnosed a at far earlier

FIG. 2. The usual outlining of the colon after administration of an enema; the terminal ileum has filled due to incompetency of the valve after the patient was turned to the prone position; the natural redundancy of the sigmoid, combined with the covering over by the coils of ileum containing barium, completely obstructs the sigmoid outline. With such roentgenograms any lesion only partially obstructing the sigmoid will be overlooked.

* Read at the Conference of Eastern Roentgenologists, New York City, Jan. 30, 1932.

FIG. 3. The sigmoid in the same case as shown in Figure 2 made with the technique described in the text. Note the clear outlining of the entire sigmoid area in spite of the redundancy.

stage, when it is possible to remove the complete lesion and before metastatic involvement is present.

A large share of the blame for existing diagnostic failures is placed upon the roentgenologist whether rightly or not, and it is his opportunity to contribute a real diagnostic aid if solution of this problem is possible. Other methods share this limitation but the roentgen ray fortunately is the usual first offender. The doctor obtaining the history from the patient often emphasizes the stomach when there is abdominal complaint. His questions, and too often his diagnosis, look toward a gastric lesion. This is only natural as the roentgen diagnosis of these lesions is highly perfected. It is a product of years of labor and thought. The colon, however, is the stepchild of this research and is dismissed with comparatively slight consideration. That it may and usually is the real cause of considerable abdominal discomfort and symptoms difficult to distinguish from involvement of the stomach seems to find little acknowledgment.

Successful roentgen examination of the colon depends on careful, painstaking and varied procedures *without* strict standardization. The usual hourly films made after a meal by mouth are unsatisfactory for visualization of the sigmoid and pelvic colon. A routine enema may also fail to outline clearly a very definite lesion of the colon. This is accounted for by several factors: the lower colon is redundant, coils on itself, is situated deeply and surrounded by the pelvic walls so that it is impossible to directly palpate or even satisfactorily visualize. By the time the large intestine is filled and the patient is turned to the prone position, the small intestine fills and further obscures the sigmoid. The result is that unless there is dilatation of the colon or other evidence of a definitely obstructive type of lesion, the pathology is covered up and unrecognized until complete obstruction has occurred.

In our experience the most satisfactory solution of these difficulties depends on *filling of the pelvic colon alone*, with ob-

FIG. 4. The sigmoid is redundant and detail is poor; the ileum did not fill.

Fig. 5. In the oblique position the sigmoid is clearly outlined throughout.

servation beneath the screen and by roentgenograms made with the patient turned in the most favorable positions to clearly outline the entire course of the sigmoid. This has been accomplished in the following manner: About one pint of opaque solution is permitted to fill the rectum and sigmoid. When the head of the column has reached the mid-descending colon or just before, the inflow is stopped and no more is permitted to enter. The patient's right

Fig. 7. A rather late stage of incomplete obstruction due to malignancy. The roentgen characteristics of cancerous encroachments are well demonstrated.

hip is elevated to a varying degree, depending on the angle at which the sigmoid is best seen under the screen. He is propped here by means of a sandbag beneath the shoulder (Fig. 1). The setting of the machine is changed from roentgenoscopy to roentgenography; a cassette is placed beneath the roentgenoscopic screen and

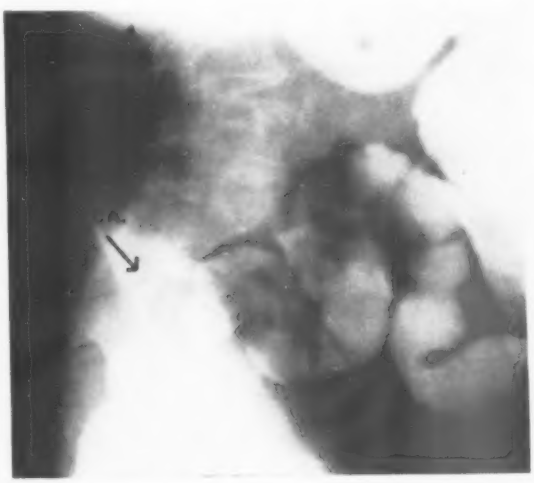

Fig. 6. An early, partially obstructing malignant involvement of the posterior rectosigmoid junction. The ragged margin was very clearly shown on the original roentgenograms and even the soft tissue mass of the tumor could be distinguished.

Fig. 8. Another advantage of this angle is the detail obtained of the lower rectum. In this case luetic involvement was suspected; on the original roentgenograms, injected opaque material was discernible in the buttock. Biopsy confirmed diagnosis of lues.

FIG. 9. Fischer's technique (barium and air insufflation) demonstrating typical sago-like or snake-skin appearance from multiple polypi of the sigmoid. Confirmed by sigmoidoscopy. No clinical symptoms.

an exposure made. Even without a Potter-Bucky diaphragm the detail will be surprisingly sharp and clear. The posterior rectal wall and entire sigmoid are well outlined (Fig. 6), and any slight irregularity of the lumen is perceptible. No obstructive lesion may be visible but the early encroachment upon the lumen by tumor or other pathology is clearly discerned when this angle is used (Fig. 6). The patient is then instructed to empty the bowel and the whole procedure is repeated. If roentgenoscopy still reveals masses of barium in the pelvic colon and rectum, a second effort at defecation is advisable. Further roentgenograms may demonstrate the mucosal folds satisfactorily (Fig. 13). Clear visualization of these mucosal folds, when possible, is of the greatest aid in study of the sigmoid and is positive demonstration of pliability of the wall of the colon. If the enema has fairly well passed out, and one must be sure this has occurred by roentgenoscopic observation, then the colon may be insufflated with air. Certain cases require this procedure, mostly those of single or multiple polypi (Fig. 9) where there has been little if any change in the intestinal wall. The procedure, however, is time-consuming and troublesome, especi-

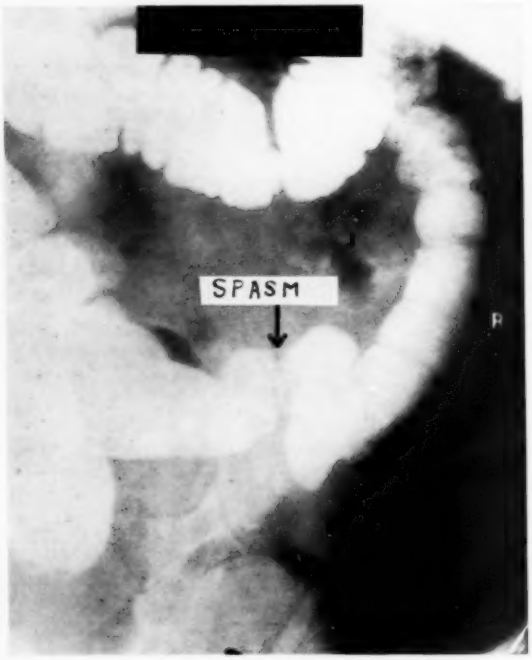

FIG. 10. An indefinite, changing deformity of the sigmoid diagnosed as spasm. Confirmed by a negative sigmoidoscopy. Patient was a physician with a history of attacks of intense pain and tenesmus with no pus or blood.

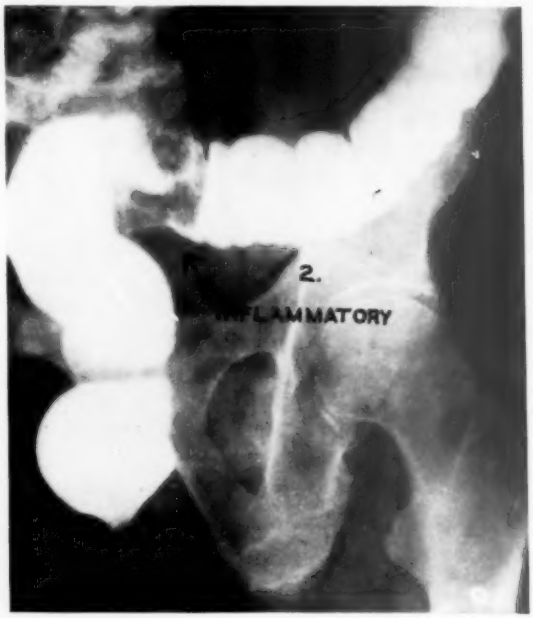

FIG. 11. Illustrating an inflammatory lesion of the sigmoid. The patient had amebic dysentery for years. This lesion had been demonstrated with practically no change in its roentgen manifestations over several years.

ally in the sigmoid, and these lesions can, as a rule, be detected by careful stereoscopic study after completely defecating the barium enema. The stereoroentgenograms taken after the combination method as advocated by Fischer,[1] if successful, are spectacular and brilliant, but are of value diagnostically only when a lesion is suspected which might be missed by the technique as described above. This is an exception rather than a rule. Air insufflation of the colon was first brought out by Cole and Einhorn;[2] later Fischer and others advocated the combination of a barium enema with injection of air. It has never been accepted as a routine procedure. Recently Weber[3] of the Mayo clinic has revived the technique. He also states that the combined method is not recommended at the present time as a routine.

FIG. 12. Diverticula are shown in greater numbers on a re-examination twenty-four hours after the enema; in this case the descending colon was involved as well as the sigmoid. The barium meal is usually preferable to demonstrate diverticula; after an enema only a few may be visible; more are usually shown in the examination after defecation and when the patient returns on the following day practically all are discernible.

FIG. 13. This case was clinically diagnosed as sarcoma of the rectum but roentgenographically the involvement was found to be extrinsic; the mucosal folds demonstrate that there is no infiltration of the wall. The sigmoid is redundant and extends to the right side of the pelvis. This roentgenogram was one of those made in the examination after defecation.

FIG. 14. The redundant, dilated lower colon is displaced upwards by the distended urinary bladder, thus bringing a malignant involvement of the sigmoid into clear view.

[1] Fischer, A. W. Ueber eine neue röntgenologische Untersuchungsmethode des Dickdarms; Kombination von Kontrasteinlauf und Luftaufblähung. *Klin. Wchsnchr.*, 1923, *2*, 1595–1598.

[2] Cole, L. G., and Einhorn, Max. Radiograms of the digestive tract by inflation with air. *N. York M. J.*, 1910, *92*, 705–708.

[3] Weber, Harry M. The roentgenologic demonstration of polypoid lesions and polyposis of the large intestine. AM. J. ROENTGENOL. & RAD. THERAPY, 1931, *25*, 577–589.

In a number of extremely difficult cases we have been successful in more clearly bringing lesions of the sigmoid to view by *distending the bladder* with air or water (Fig. 14).

Using a selected technique for each case one may show by characteristic filling deformities ulcers in colitis as well as the stiffened wall of the intestines.

After thorough study is made of the lower colon, the upper may be filled with a second enema and the usual examination performed.

SUMMARY

Examination of the colon by means of oblique roentgenograms and roentgenoscopy is a well-established routine procedure which has been in use for many years; in spite of routine use of such procedure malignant and other lesions of the sigmoid are overlooked. The coils of terminal ileum which contain barium, the low position of the cecum as well as a redundancy of the sigmoid itself contribute factors which are almost insurmountable unless partial or complete obstruction has already taken place. Oblique films of the sigmoid *when only the pelvic colon contains barium* overcome these defects and permit more exact diagnosis. The sigmoid, posterior rectum and anal region are clearly outlined by this method and clear detail is obtained of the entire redundant sigmoid. We hope that when as much effort is spent in the roentgenological examination of the pelvic colon as is now spent in that of the stomach, the diagnosis of the early lesions of the sigmoid will be perfected.

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WORK IN THE FIRST DECADE OF ROENTGENOLOGY

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ON FIRST hearing of Professor Roentgen's great discovery of the x-rays late in 1895, I was naturally deeply interested. Many years before, I had obtained a number of Crookes vacuum tubes, exhibiting the effects of so-called radiant matter or cathode rays, but until Roentgen's discovery, it was not known that such tubes gave out any rays into the surrounding space. The phenomena, luminous, thermal and mechanical, were supposed to be limited to the interior of the tubes, or, at least, to be unaccompanied by any radiation into the surrounding space.

Early in 1896, I examined these Crookes tubes to discover, if possible, which form was best suited for roentgen-ray examination, and further, the more important knowledge of what part of or in what condition the interior of the tube was favorable as a source of the rays. In short, I aimed to discover the most effective form of tube for roentgen-ray production. It was soon determined that the place of impingement of the cathode rays was indeed the locus of roentgen-ray emanation. I found among my tubes one in which a concave cathode cup was, as it were, focussed upon a strip of platinum at or near the center of curvature of the concave cathode. It was found also that nearly all the roentgen-ray emanation from that tube came from a small heated spot on the platinum strip or plate, and that sharp shadows were produced on a fluorescent screen or photographic plate of the bodies more or less opaque (to rays), exposed thereto. The anode connection, it was found, could be made to the platinum plate itself or to a separate anode terminal within the bulb or tube (see Fig. 1).

Figure 1 is a fairly exact drawing at one-half scale of the tube itself in condition to produce the rays, which tube I still have. Having at command both static machines and Ruhmkorff coils for excitation, one or the other could be employed for the electric discharges through the bulb or tube, as desired, the coil being found, on account of its greater output, more effective. In my eagerness to experiment with this tube, it was accidentally broken down by perforation near the seal and rendered useless soon after it had been operated. This was indeed a great loss, as none of the other Crookes tubes were effective in furnishing rays properly directed for experimentation. To remedy this loss, I at once set up a Sprengel vacuum pump—after repairing by the glass-blower's lamp the cracked part of the tube—and in a night and a day

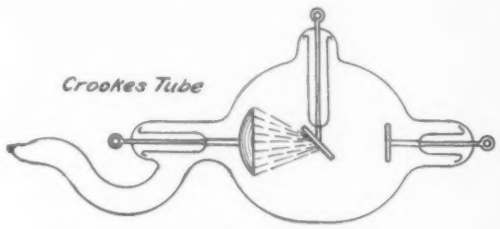

FIG. 1

the exhaustion, to the high vacuum required, was completed, with this remarkable tube again in service.

It having been definitely settled that the type of tube just described was superior to all others tried at the time, arrangements were made to duplicate the tube with minor modifications, leading to proposed standard tubes, such as the double focus tube to be used with alternating current discharges from transformers giving the requisite potentials.

In the course of these early experiments, certain important facts were discovered. For example, it was found that the rays could penetrate many sheets of sensitized paper, and that shadow images could, on development, be found on each as manifolds. Another development was the production of stereoscopic roentgen pictures, such that in bone fractures and the like, the exact relation in space of the surfaces of

the bones could be seen, and measures taken to secure the precise position and alignment, so that in healing there could be no displacement or deformity. These were produced for the first time early in 1896. Another set of observations concerned the power of the rays to set up

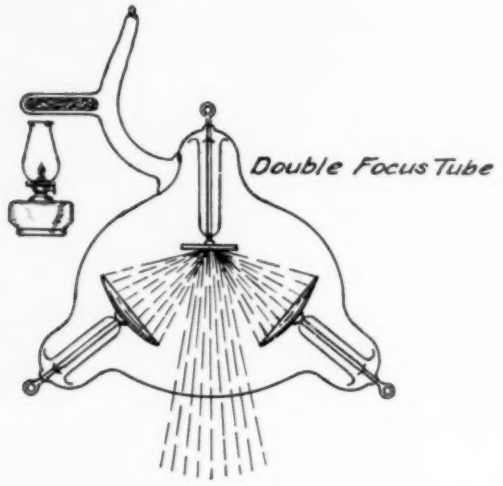

FIG 2

secondary emanations in bodies like wood, paraffin, etc. These secondary rays were less penetrating and were radiated in all directions from the body subjected to the initial ray source. I carried these investigations still further and found that the secondary rays or emanations would themselves excite still further diffusions which were termed "tertiary." These were suspected as still softer or more readily absorbed than the secondary rays. It was seen that these phenomena could be regarded as akin to the excitation of fluorescence or phosphorescence by ordinary light rays, or perhaps were somewhat representative of the fluorescence excited in some substances by ultraviolet rays of the spectrum, that is, by the invisible rays, an action which seems coincident with a lowering of pitch or reduction in the pitch or vibration rate.

There were two serious misconceptions in the early days which tended to do harm and to need emphatic correction. It was claimed by some that the roentgen rays themselves were innocuous, and that any injury by them was to be laid to the electric discharges or changes of electric conditions affecting the skin and tissues. It was also claimed and believed by many that tubes excited by static machines, so called, would not produce injury, while those operated from induction coils were far more likely to produce injury. These ideas were shared by some authorities who should have known better.

It was on this account that in the latter part of 1896 I deliberately determined to make some crucial experiments and publish the results. To this end, shielding by a lead sheet my left hand, with the exception of about 1 1/4 inches of my little finger, I exposed the unshielded end of the finger close to a tube yielding rather soft rays, for twenty minutes. Also, to clinch the matter, I used only a static machine discharge to excite the tube. At the ninth day after the exposure, the finger where it had been exposed was inflamed, and on the eleventh day the exposed skin was necrosed and shed. The burn took a long time to heal, and then only by a new scar growth from the sides. Several articles were published at the time calling attention to the extreme danger. In spite of the deliberation I used, I have seen this burn of mine erroneously described as the result of an *accident*. Finally, on the next finger to the one so burned, and in order to settle absolutely that the injurious effect was due not to electric effects, but to the rays themselves, I cut an elongated oval in a sheet of lead, shielding the most of the finger with it, leaving for exposure the long oval, which was, however, divided into three sections. One of these was bare, or fully open, unshielded. Another part was covered with heavy tin and lead foil (tin foil), and the third with thin aluminum foil, a perfect shield electrostatically, but transparent to the roentgen rays. After exposure, the part covered by the tin foil was free from any injury—no redness nor inflammation showing at any time—while the unshielded part of the finger was burned, and also

the skin under the aluminum foil, thus setting at rest any possible doubt that the rays themselves were the true cause of the lesions. Of course, subsequent history fully confirmed these early findings, but a note of warning was indeed needed at the time.

There has been a serious misconception as to the bearing of the work of Mr. Herman Lemp on the art of excitation of roentgen-ray tubes. Mr. Lemp was a coworker with myself in the early days of roentgen-ray development, and it was he who devised what we termed the Lemp selector, which, so far as I know, has become the standard apparatus for delivering the rectified energy to the various forms of roentgen-ray tube, such as the famous Coolidge tube. Discarding both the static machine and the induction coil, Mr. Lemp, in the laboratory of the General Electric Company at Lynn, Massachusetts, organized a high tension rectifier, in which the high voltage discharge from an oil-immersed step-up transformer was controlled by a revolving connector or selector to cut out the half waves in one direction and send to the roentgen tube only those of the other direction, so that the discharges through the roentgen tube should be unidirectional. The success of this apparatus led us to abandon the static machine, as well as the induction coil, for heavy work. The selector or revolving switch in the Lemp apparatus was driven by a small synchronous motor on the same source as the primary of the step-up transformer.

The Lemp selector is described in his U. S. patents Nos. 774,090 and 774,138, as applied to *x-ray tube excitation only*. It was invented for that purpose only. It was used by us for the same purpose only, and there is certainly no need to ascribe its application to roentgen-ray work to anyone else. The only figures in his patents show application to x-ray tube excitation only. It gave us such great power even in the early days long before 1904, when the patents were issued, that we were able to bring to a white heat in a few seconds a target of iridio-platinum 1 inch square and 1/16 inch thick. In fact, we had to cut down the energy in the tube circuit by a resistance, usually a rubber tube several feet long filled with water in circuit with the high tension secondary of the transformer.

I have disgressed to show the importance of the Lemp selector invention, and its bearing on the art and its early invention to date, because some statements I have seen in print seem to indicate that, in the belief of the writer responsible for them, it received its adaptation to roentgen-ray use long after its invention, when, in fact, the Lemp invention was made *for x-ray use* and no other, as clearly shown in the patents themselves.

I remember well that in these early experiments with the Lemp selector and a fluoroscopic screen for observing, the shadow of a leaden bullet of about 1/2 inch diameter was seen clearly through iron plates of not less than 1 inch total thickness. It was in this connection that I found the method described in my patent #500,630 for obtaining from a D.C. current of alternating currents of desired frequency by shunting an arc with an inductance and capacity in series and varying at will these factors This method was afterward discovered in London, England, by Duddell and called the "singing arc." It was also applied in wireless telegraphy under the name of the Poulsen arc, but the principle and mode of operating were discovered in our Lynn laboratory earlier than July 18, 1892, the date of application for the U. S. patent referred to. It may be mentioned that in connection with this work, high frequency apparatus of great power was made, some of which was shown in operation at the World's Fair in 1893 at Chicago.

The coreless, oil-immersed, high frequency induction coil came into existence at our laboratories some years before Roentgen's discovery of the x-ray, and it was found that a full horse-power of energy could be delivered to the body from hand to hand through the chest without any

other apparent effect than heating the tissues, particularly at the wrists.*

Early in the working of roentgen-ray tubes, it was found that the degree of vacuum gradually rose until it was too high to pass the current, since the evolution of cathode rays from the cathode within the tube depended on the presence of gas molecules. The tube became hard, the rays more penetrating—which, for certain work was disadvantageous— and the potential required to work the tube rose. There was, as a consequence, need of a vacuum regulator, one form of which came into existence just prior to August 21, 1896, the filing date of patent #575,772, issued January 26, 1897, which describes this type of tube, and patent #591,899 of October 19, 1897, filed August 4, 1897, which is a modification wherein the regulation of the tube is accomplished automatically. The later invention of the Coolidge tube rendered these devices unnecessary, since Coolidge's excellent step in progress required that the roentgen-ray tube should, in its construction, be given a very high vacuum or be made as "hard" as possible; the hot cathode coil in the tube being relied upon for the emission of the cathode rays for impingement on the target, which latter was made massive, of tungsten, and provided, as needed, with means for cooling or carrying off heat.

Naturally, the progress in the development of means for obtaining and controlling roentgen rays, since the work briefly alluded to in the foregoing, has been very great, with the creation of an art based on Roentgen's discovery in 1895, which has been of invaluable service in clinical work.

The brief record of some of the more interesting of the early phases of the work in which I was engaged, might, of course, be enlarged and extended to a considerable degree, by records of tests made and apparatus tried, but it is thought that the foregoing story may be of interest so far as it embodies some of the most important of the steps taken in experiments and discovery.

* Effects of high frequency electrical discharges passed through the body. *Tr. Am. Electr. Therap. Ass.*, Sept. 27, 1894.

SPECIAL RAILROAD RATES

ALL MEMBERS AND GUESTS who anticipate attending the Detroit Meeting of the American Roentgen Ray Society in September are requested to purchase one-way tickets and ask for Convention certificate at that time. If one hundred certificates are presented, return tickets may be purchased at one half of the regular one-way fare.

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THE OSSIFICATION IN THE EXTREMITIES OF THE NEW-BORN

By THOMAS O. MENEES, M.D., *and* LELAND E. HOLLY, M.D.
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GRAND RAPIDS, MICHIGAN

WHILE the new-born knee, foot and wrist have been extensively studied, the shoulder and hip have been neglected. As epiphyses appear in these regions in the first year, it seemed probable that they might be present occasionally at birth. The elbow was included for completeness.

The upper and lower extremities of 640 infants were examined in the first forty-eight hours of life, the large majority in the first twenty-four hours. All children born in this hospital during the study were included. The films of 140 of these were discarded for various reasons. This left 500 cases, all over 2 kg. in weight and 39 cm. in height, and with a menstrual age of at least 255 days. Of these 263 were males and 237 females. This group would represent a fair average for new-born infants in this country with one exception, that only two were negroes. All of the exposures were made in one-tenth second or less, with double intensifying screens.

Table 1 shows the frequency of appearance of the different centers of ossification. The number of appearances of ossification in the head of the humerus and coracoid process of the scapula was surprising. In addition to the tabulated bones, the elbow was examined but showed no epiphyses.

Bony centers were present in the carpus in 48 cases. Both capitate and hamate were present 32 times. The capitate was present alone 9 times and the hamate alone 7 times.

In the foot the centers for the calcaneus and astragalus were present in all cases. The cuboid showed a greater tendency to arise from multiple centers, as noted by Adair and Scammon.[1]

As expected from the work of Pryor,[2] females showed a higher percentage of epiphyses than the males. This held true in all regions except the upper epiphysis of the tibia, where the incidence was practically equal. With increasing weight, length and menstrual age the percentage of epiphyses present increased roughly but did not run exactly parallel.

The development of the two sides was largely symmetrical. Unilateral appearance

[1] Adair, F. L., and Scammon, R. E. A study of the ossification centers of wrist, knee and ankle at birth, with particular reference to physical development and maturity of the newborn. *Am. J. Obst. & Gynec.*, 1921, *2*, 35.

[2] Pryor, J. W. Differences in the time of development of the centers of ossification in the male and female skeleton. *Anat. Rec.*, 1923, *25*, 257–268.

TABLE I
FREQUENCY OF APPEARANCE OF CENTERS OF OSSIFICATION

	Male		Female		Both Sexes	
	No.	Per cent	No.	Per cent	No.	Per cent
Head of humerus	122	46.4	112	47.2	234	46.8
Coracoid	28	10.6	32	13.5	60	12.0
Capitate	10	3.8	31	13.0	41	8.2
Hamate	11	4.1	28	11.8	39	7.8
Elbow	0	0	0	0	0	0
Head of femur	1	0.3	2	0.8	3	0.6
Lower epiphysis of femur	259	98.4	236	99.6	495	99.0
Upper epiphysis of tibia	212	80.6	191	80.6	403	80.6
Cuboid	92	35.0	133	56.5	225	45.0
III cuneiform	1	0.3	9	3.8	10	2.0

Table II
ASYMMETRICAL APPEARANCE OF EPIPHYSES

	Male	Female	Both Sexes
Head of humerus	8	6	14
Coracoid	4	3	7
Capitate	1	1	2
Hamate	1	0	1
Lower femur	1	0	1
Cuboid	3	3	6
External cuneiform	1	0	1
	19	13	32

of an epiphysis occurred 32 times in this series (see Table II). In only one individual did more than one asymmetrical epiphysis occur. This was a female with centers for the head of the right humerus and right cuboid. Lack of symmetry was slightly more frequent in the male than in the female. It was 3 times more frequent in the upper than in the lower extremity. The right epiphyses appeared more frequently than the left (21 right and 11 left).

Of the 31 infants with a unilateral appearance of an epiphysis only 11 could be traced for a sufficient length of time to determine whether they were right- or left-handed. The hand used by preference agreed in 9 with the side on which the epiphysis first appeared (see Table III). In 3 cases, where epiphyses were present on both sides, but one larger than the other, the larger epiphysis was on the side used most.

The average sequence of appearance of the centers was as follows:

1. Lower femur
2. Upper tibia
3. Head of humerus and cuboid
4. Coracoid
5. Hamate and capitate
6. External cuneiform
7. Upper femur.

As noted by Adair and Scammon, the centers of knee, foot and ankle followed a regular sequence. The epiphyses of the shoulder show a wide variation in their time of appearance. The center for the coracoid can appear before the head of the humerus and both can appear before the cuboid.

Table III
RELATION OF UNILATERAL CENTERS TO RIGHT- AND LEFT-HANDEDNESS

	Unilateral Center	Hand Used	Agree	Disagree
Female B	Left head of humerus	Left	—	
Male S	Right head of humerus	Right	—	
Male E	Left cuboid	Left	—	
Female S	Right head of humerus	Right	—	
Female C	Head left humerus	Left	—	
Female H	Right coracoid	Right	—	
Male W	Left cuboid	Right		—
Female F	Right coracoid	Left		—
Male L	Right head of humerus	Right	—	
Male J	Right cuneiform	Right	—	
Female F	Right head of humerus and right cuboid	Right	—	
			9	2

A SHUTTER GRID PERMITTING PLURAL RECORDS UPON THE SAME FILM*

By HAROLD THOMAS, M.D.
BOSTON, MASSACHUSETTS

IN A previous paper[1] I presented a simple technique whereby the outlines of the diaphragm at the limits of its excursion in expiration and inspiration may be registered upon the same film. This was attained by taking advantage of the protection offered by the shifting soft tissues and altering the film-blackening factors so that records of the two positions might be preserved. In general, success in the technique consists in greatly limiting the time, voltage or wave-length factor during the exposure of the organs in inspiration, over that in expiration, the sum total of the exposures to be well within the capacity of the film. When, with other factors remaining constant, the time for each exposure was equal, those moving elements, as the ribs, not protected by tissue densities, were equally well shown; but as the ratio increased for the expiratory phase and diminished for inspiration, the contrasts of the shadows of the diaphragm and heart became progressively better until a ratio of seven for expiration to one for inspiration, with portable technique, was reached.

This method has already proved to be a valuable adjunct in checking up the movements of the diaphragm in postoperative conditions. Throughout the hospital with portable apparatus of various types, uniformly good records have been obtained.

The technique is very satisfactory where the diaphragm has moved physiologically. However, instances have frequently arisen where the diaphragm has moved little or not at all, or the movement has been paradoxical. Under these conditions but one diaphragm outline is seen and the observer is at a loss to know whether there has been an error in technique, or actually some abnormal condition is present. To obviate this confusion, it seemed necessary to depart from this method of superimpos-

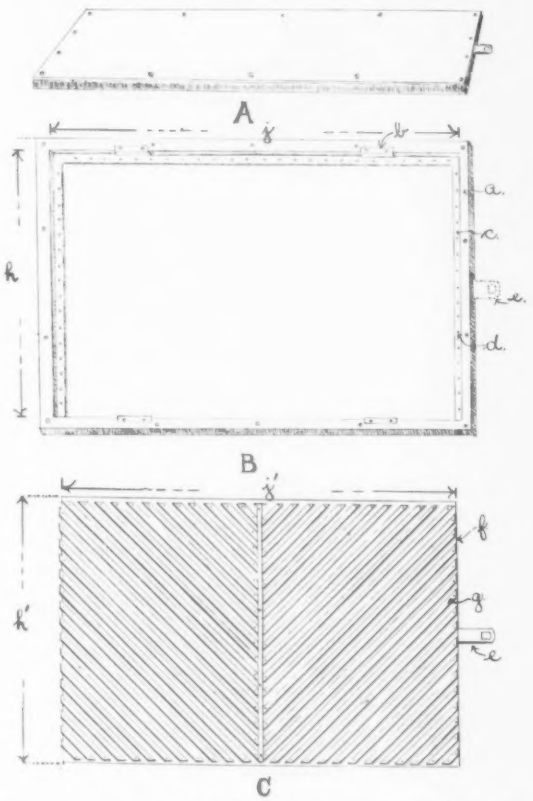


FIG. 1. A. Shutter grid complete in its housing. B. Housing with cover and grid removed. a. Frame. b. Cleats to hold the grid in sliding engagement. c. Lead plate serving as a bed for the grid and bearing as a marking device holes, d. d. Holes 1/16 inch in diameter, which in one position of the grid are open and in another are closed by the lead bars. e. Position of the handle of the grid when in place. h. The internal width of the frame. j. The internal length of the frame.
C. The grid. f. Aluminum plate. g. Lead bars (set up with lead rivets) of equal dimension and spaced from each other by the dimension of their own width. h′ is the same width as h. j′ the length of the shutter grid. This is less than dimension j by the width of the lead bar at its cut end.

[1] Thomas, Harold. A graphic method of recording the respiratory excursion of the diaphragm. AM. J. ROENTGENOL. & RAD. THERAPY, 1931, *26*, 878–880.

* From the Department of Roentgenology, Massachusetts General Hospital, Boston.

ing views and to provide for each position of the diaphragm a separate unexposed area on which to register. Thus the problem became one of splitting the film into two sets of sections, each set of which might be alternately exposed in one phase and protected in another. The tissue contours would then be viewed as through a picket fence. In order that they might be completely traced, the divisions of the field would need to be small and so placed that they would not run tangent to the parts under consideration.

In devising an instrument to meet these requirements, three elements were essential:

1. A grid, consisting of a series of parallel bars of material highly absorptive for roentgen rays, mounted upon a form easily penetrated by them, the impermeable bars to be of uniform size and spaced from each other by the dimension of their own width.

2. A housing element made of materials easily penetrated by the roentgen rays to contain the grid and allow sufficient play to it in one direction to permit the opaque bar to cover the space adjacent to it.

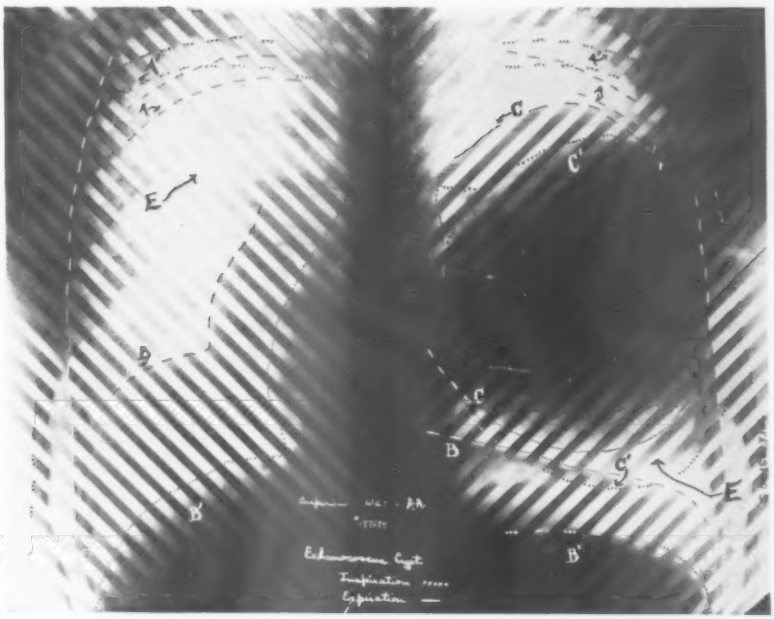
3. A marking device which would identify upon the film the position of the grid at a given exposure.

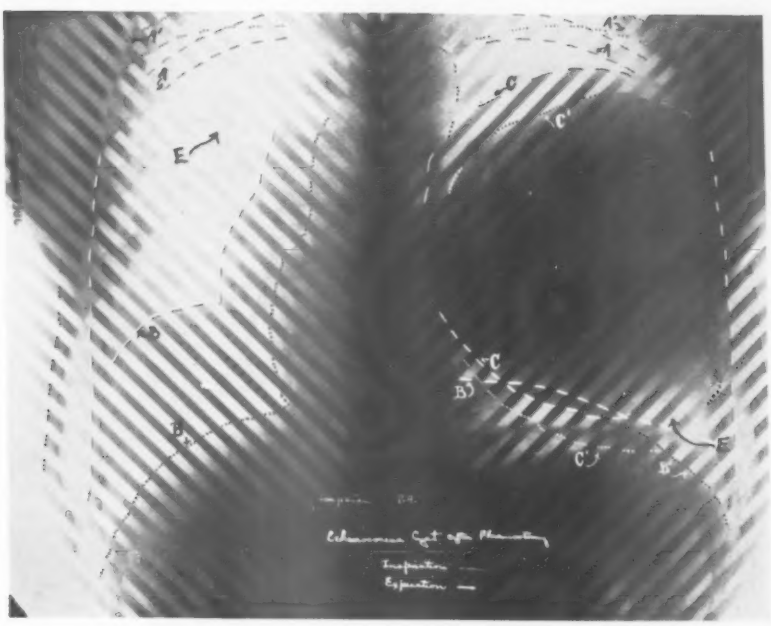
In meeting these demands, an instrument was prepared as follows:

The Grid. Upon a plate of aluminum 0.060 inch in thickness there was set up a system of lead bars.* These bars were 1/12 of an inch in thickness and 1/6 of an inch in width, and were spaced 1/6 of an inch apart. It was essential that one should avoid having the bars run tangent to important tissue contours in order to pick up with accuracy the slightest movement. Therefore the bars were arranged to extend laterally about a central spine at an angle of 45°. As

FIG. 2. Female, aged fourteen. Appendectomy; general peritonitis. Ten days after operation marked elevation of temperature and leucocyte count. Subdiaphragmatic abscess suspected but ruled out by grid picture demonstrating positive movement of both domes.
A–B. Position of ribs and diaphragm respectively in expiration.
A′–B′. Position of ribs and diaphragm respectively in inspiration.

* Narrow bars of this dimension were made practicable through the use of "printers' leads." These contain about 10 per cent of antimony and thus possess considerable rigidity as compared with pure lead. It was therefore possible to rivet them to the aluminum plate with great accuracy.





FIGS. 3 and 4. Echinococcus cyst, before and after phrenectomy (left).
A, B, C. Position of ribs, diaphragm and cyst respectively in expiration.
A′, B′, C′. Position of ribs, diaphragm and cyst respectively in inspiration.
It is interesting to note that the expiratory bars in the left costophrenic angle are of lesser density than the expiratory bars over the uninvolved lung, demonstrating localized emphysema.
E indicates the expiratory phase.

this "spine" in the examination of the chest would come over some of the dense mediastinal portions where movement could not be recorded, obscurity produced there by its double outline could be ignored. The strips of lead were fastened in position on the aluminum plate with lead rivets and the length of the plate was cut to allow an end play of 0.234 inch which would permit the bars in the shift to occupy the adjacent spaces. An extension of the aluminum plate was passed out through one end of the frame to serve for a handle to operate the grid.

Housing Element. For this an old cassette was utilized, such as is commonly used with the 11×14 inch intensifying screens, the back of which was missing. Over the back of the frame a piece of bakelite was cut to come flush with the outer edges and fastened down with screws, to permit easy removal. In the middle of one side of the frame a slot was made to allow for the passage of the handle of the grid.

Marking Device. Across the ends of the cassette and along one side a narrow band of lead and antimony alloy was attached with lead rivets to the inner aluminum face, close up to the frame. Through this strip holes 1/16 of an inch in diameter were placed uniformly apart from each other in such a manner that they would appear in one position of the grid upon the film and be obscured by the grid itself in the other position. These lead strips served also as a bed upon which the grid should move.

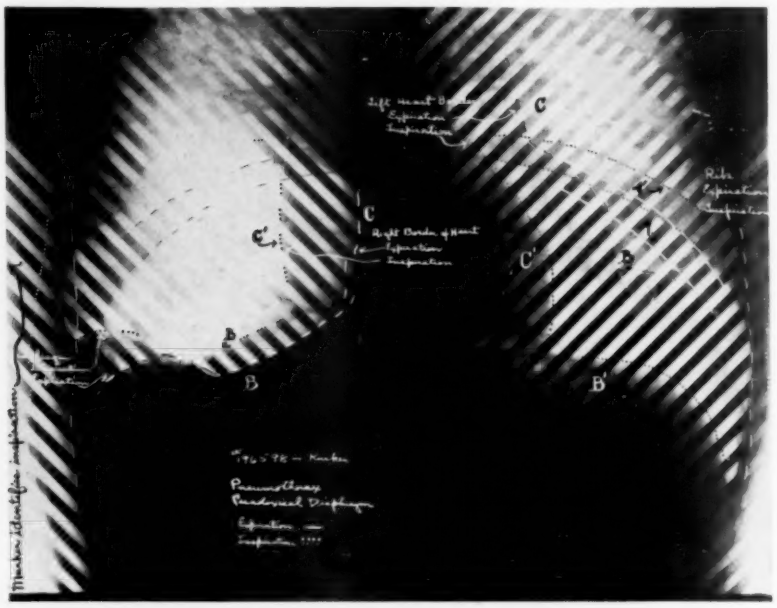


FIG. 5. Male, aged thirty-five. Tuberculosis for five years. Artificial pneumothorax maintained for two years. Partial collapse of the right lung.
A, B, C. Ribs, diaphragm and heart contours in expiration.
A′, B′, C′. The same structures in inspiration.

Method of Use. To record movements of the heart, diaphragm and ribs in respiration the instrument is placed upon a film-holder or cassette beneath the patient's thorax. The handle of the grid is pushed in completely, opening the holes in the marking device. An exposure is now made in full inspiration. The grid handle is drawn out to the limit of its range of movement and an exposure made in expiration. In the second position, the lead bars have moved to occupy their adjacent spaces and the marker is closed.

Interpretation of the Record. Upon development there is found what at first appears to be a conglomerate mixture of densities. With a little practice, however, especially where there has been normal physiological excursion, it is possible to pick up the alternating bands of the two positions and view them separately. One may determine the phase of movement as represented by a given contour by referring to

FIELDS OF USE

Chest:

Diaphragm. With this instrument the position of the diaphragm may be demonstrated whether fixed, moving slightly, normally or paradoxically.

Diaphragm and Ribs. A permanent record may be made showing the relative movement of ribs and diaphragm in following the progress of chronic pulmonary con-

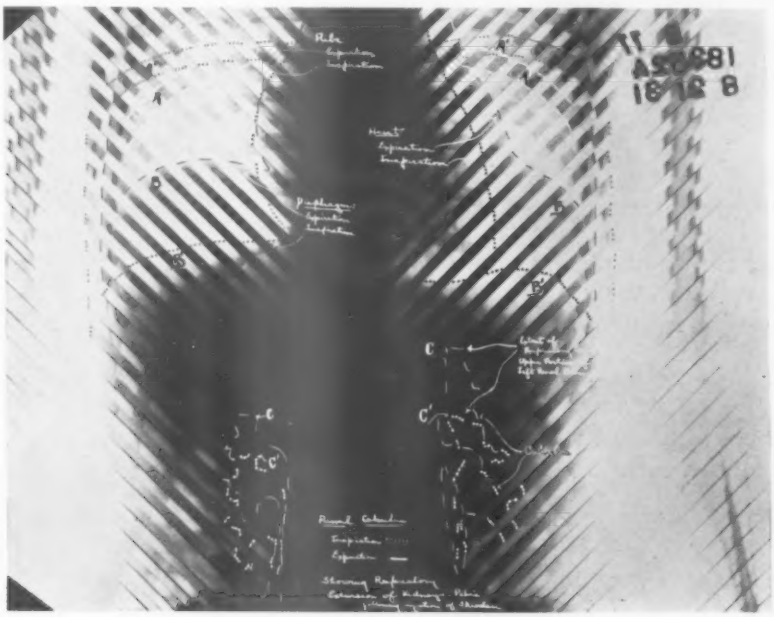


Fig. 6. Female, aged eleven. Renal calculus. Pelves of kidneys demonstrated after injection with skiodan —showing here the amplitude of excursion on forced respiration.
A, B, C. Position of rib, diaphragm and renal pelvis in expiration. A′, B′, C′. Position of same structures in inspiration.

the marker whose openings appear on the top and sides of the film.

Where there is doubt concerning the movement present, one is aided by the use of a mat which will obliterate completely one of the views. Such a mat may be prepared by exposing a film beneath the grid itself. This may be placed over the film with the opaque bars covering the bands of exposed film bearing the round marker, and there will be observed a picket-fence view of the lung in expiration. Then by shifting slightly to one side, so that the opaque mat allows the markers to come in view, one attains only the inspiration contours.

ditions, as in artificial pneumothorax, where roentgenoscopy may be neither available nor advisable.

Lung. If the same exposure setting is used for expiration as for inspiration, there will appear side by side across the lung fields considerable contrast of density between the two bars. In the presence of emphysema or atelectasis this element of contrast will be almost negligible. Tumors of the lung and chest wall may be outlined in their limits of respiratory excursion, thus affording data for the determination of their character and localization.

Heart. The respiratory ballottement of

the heart between the diaphragm and the great vessels may be clearly demonstrated. The character of this movement will naturally be affected not only by the state of the heart itself but by that of surrounding organs and supporting structures.

With a device to assure the exposure of the heart in systole and diastole records may be obtained, upon the same film, of the amplitude of contraction and relaxation of heart and aorta. Expansile tumors—as aneurysms—of the great vessels may be demonstrated and recorded for evidence of progress of the disease.

Abdomen:

With the improving technique for the visualization of the gallbladder and kidney, this method makes possible a record of the movement of these organs during respiration and change of posture.

Localization of Foreign Bodies:

As there is presented here the opportunity of making separate exposures upon the same film, it should prove of value in localizing foreign bodies which are invisible by the roentgenoscope.

Relation to Roentgenoscopy:

While these fields of use appear to present little which is not already available by roentgenoscopic examination, such an instrument possesses the following advantages:

1. It affords a roentgenographic record of movement, thus avoiding the danger of optical illusion so often arising during roentgenoscopy amid a mass of shifting contours.

2. It makes possible a record of diaphragm, rib and heart excursions where roentgenoscopic examination at present is difficult as well as dangerous for the bedridden patient.

3. It presents an opportunity to analyze the alteration in shape and position of thoracic organs in two different aspects.

4. It affords a permanent record of the amplitude of organic excursion and presents an aid in observing the progress of chronic thoracic states.

5. It allows a roentgenographic record of the comparative densities of lung tissue in expiration and inspiration.

SUMMARY

An instrument is described which permits the splitting of the roentgenographic film for exposure into separate series of sections and operates so that each series is alternately exposed to and protected from the roentgen rays.

With a marking device provided to identify each exposure, separate records of tissue contours may be obtained upon the same film.

Some of the fields for its use are suggested and its possible advantages over the roentgenoscopic method are outlined.

I am indebted to the Boston Gear Works for their kind cooperation in the preparation of this instrument, especially to Mr. E. Toagus, in the experimental department.

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EDITORIALS

CAUSES OF CELL DEATH IN IRRADIATED TISSUE

WHEN one is working on a limited problem or investigates a problem from a limited point of view or with material largely of one kind, unwarranted deductions may easily be made. This is especially true when the field is broad and the problem under investigation constitutes only one phase of it. The cellular alterations occurring after exposure to roentgen rays or radium have been investigated by a large number of workers, and the changes noted have been described from the standpoint of the clinical and pathological effects on animals, the purely pathological effects on human beings as shown by sections of tissue removed after irradiation of benign and malignant lesions, and also from the clinical standpoint of the therapeutic radiologist. The results obtained and the conclusions drawn by various workers have often differed according to the experimental conditions or according to the material on which the observations were made. A deduction based on observations from any one of the foregoing standpoints may be fully justified by the facts or may be more or less misleading as the author has kept the deductions within the scope of the experimental, pathological or clinical findings or may have allowed the deductions to imply or to state more than the observations really warranted.

An interesting example of the tendency to unwarranted interpretation of facts is to be found in a recent number of the *Journal of Pathology and Bacteriology*.* In a most interesting article entitled "Causes of Cell Death in Irradiated Human Tissue," Doctor B. D. Pullinger (Clinical Pathologist, The Mount Vernon Hospital, Northwood, Middlesex), having observed in and around different kinds of irradiated malignant tissues vascular (especially venous) dilatation and hyperemia, thrombosis and necrosis of blood platelets, exudation of serum and rupture of blood vessels with subsequent fibrosis and pressure atrophy, ventures to advance the hypothesis that the destruction of benign or malignant cells by radium or roentgen rays is due, not to a primary, specific and direct action of the rays on the cells themselves, but to interference with the blood supply of the cells through thrombosis, infarction, etc.

As such, Pullinger's communication and her observations of tissue changes induced in and around tumors by irradiation are of the greatest value, because they illustrate quite clearly that the outstanding effects of implanted radium seeds or needles, of surface application of the radioactive agent, or of external irradiation at a certain distance with the so-called radium bomb, are vasodilatation affecting the capillaries, veins and arteries, marked hyperemia, and clumping of the corpuscles and platelets. These changes are more pronounced in the capillaries and veins than in the arteries and also depend on the character of the supporting connective tissue. The fact that "vessels in a loose, delicate stroma . . . appear to be more readily affected than those in dense fibrous tissue and collagen" explains why mucous membranes are prone to greater hyperemia than the corium of the skin. In tissues adjacent to the affected vessels edema and wide separation of cells and fibers were noted, and desquamation of the overlying epithelium was attributed to the edema. Vasodilatation in irradiated tissue was said to be followed by thrombosis of platelets and later by separation of

* July, 1932, 35, 527-540.

fibrin, and this "may extend till sufficient vessels are occluded to produce necrobiosis or infarction." After irradiation of the uterine or cervical mucosa, the thrombosis causes the whole mucous membrane to undergo coagulation necrosis and to slough away. Extension of the process was described as leading to loss of the surface epithelium and thus as opening the way to infection. Similar thrombosis and anemic necrosis were noted in voluntary muscles and bones in or adjacent to the irradiated areas. Degeneration of endothelial cells was found only in large veins and arteries and was ascribed to arrest of circulation in the capillary area. The endothelial damage was regarded as mechanical and "probably due to loss of elasticity, owing to the very great stretching these cells undergo." Actual rupture of vessels was often observed, and blood cells and serum had seeped into the connective tissue spaces. The extravasation of blood and exudation of serum also were held to cause the death of cells, especially in voluntary muscles. Repair of the injury was found to proceed by removal and organization of the dead material, by proliferation of macrophages and phagocytosis, by infiltration of lymphocytes and plasma cells, and by proliferation of young capillaries and fibroblasts. The final scar was described as acellular, non-vascular, and as containing a large quantity of elastic fibers. When, during the early phase of reaction, many larger vessels have thrombosed, healing may not take place, and an area of quiet necrosis may persist indefinitely.

Essentially similar observations were made in malignant growths, in adjacent non-malignant tissue, and also in some experiments on rabbits in which the irradiated skin of the groin remained unaffected, but the vessels supplying the bladder, hilum of the testis and vas deferens became greatly engorged and thrombosed. Morphological changes in endothelial cells were not perceived, but degeneration of seminiferous cells, similar to that described by Bergonié and Tribondeau, was observed.

As far as the pathological findings are concerned, they agree in the main with those of many other investigators, but when it is deduced that the vascular changes previously described account for all radiation effects, when the direct action of radium and roentgen rays is questioned and the conclusion is drawn that "all effects following irradiation are related to . . . vascular stimulation and vascular degeneration," the tendency of the author to read into her observations implications far greater than the facts justify becomes evident. Moreover, other evidences of this tendency are to be found throughout the paper.

The pathological data furnished by Pullinger undoubtedly are an accurate representation of the cellular and tissue changes found at certain stages after irradiation, and to this extent they cannot be questioned. However, they do not necessarily substantiate the view that hyperemia is the first effect of irradiation. It may have been the earliest alteration perceptible at the time the tissues were examined, but this is quite a different matter. It is well known to pathologists that hyperemia usually results from any irritation of cells and tissue, including the blood vessels themselves, although the primary irritation may be, and often is, independent of the vessels. One point deserves notice. This is that, although roentgen rays were mentioned as inducing similar effects, most of the pathological data supplied by Pullinger were based on organs and tissues exposed to radium for malignant tumor. This implies the strongest possible doses consistent with the relative tolerance of adjacent normal tissues. Also in the experiments by others, cited by the author to fortify her case, the method of employing radium usually was such as to make vascular changes practically unavoidable. But to anyone familiar with the experimental evidence as a whole, especially when this is supplemented by extended clinical experience, Pullinger's contention that irradiated cells die always as a result of vascular hyperemia, throm-

bosis, infarction, rupture of vessels, extravasation of blood, exudation of serum and edema does not appear strong. These factors undoubtedly account for the death of cells to a certain and perhaps considerable extent, but certainly not all the cells that perish after irradiation are destroyed in this way. Full or tolerance doses of radium or roentgen rays cannot furnish a satisfactory answer to the question of direct or indirect death of cells. In other words, evidence of direct action on cells cannot be obtained by doses sufficient to injure more or less indiscriminately all the tissues in the irradiated territory or by examining such tissues only after the cycle of radiation changes has largely or completely run its course.

In the experiments on rabbits, undertaken by Pullinger to elucidate the problem, a suberythema dose was given to the inguinal region, and the five animals were killed seven, fourteen, fourteen, twenty-one and twenty-eight days, respectively, after exposure. The fact that changes in the skin of the exposed area could not be found, while the vessels supplying the bladder, the hilum of the testis and the vas deferens were greatly engorged does not prove that the cellular degeneration in the seminiferous tubules was the result of the vascular dilatation, hyperemia and thrombosis. With equal and perhaps greater justice it can be argued that the vascular phenomena were secondary to degeneration and destruction of the seminal epithelium. Moreover, a smaller dose of radium or earlier examination of the tissues (three or four days after exposure) would probably have shown degeneration and desquamation of spermatogonial cells, with little or no hyperemia.

The evidence in favor of direct action of the rays on cells and tissues is so abundant and strong that such action can be regarded as absolutely established. It must not be inferred that indirect destruction of cells, through vascular disturbances such as Pullinger has described, does not occur. On the contrary, such destruction undoubtedly plays a part in the radiation effect. When the dose of rays is relatively small, certain varieties of cells may be destroyed and hyperemia may occur only as a secondary, compensatory, or reparative effect. On the other hand, when the dose is great enough, a direct action on all kinds of cells, including the cells of blood vessels, may occur as a primary effect, and, if the changes are sufficiently pronounced, secondary or indirect destruction of other cells also may result.

In a way Pullinger is quite right in questioning the selective action of the rays. It is not the rays that have the power or property of selecting the cells or tissues to be injured or destroyed. The rays are quite indiscriminate in their action. The selection is done by the cells themselves, different species of which are influenced more or less rapidly by the same dose or to the same extent by larger or smaller doses according to their natural susceptibility, that is, according to the rate of metabolism of each kind of cell and the metabolic stage at which different cells of one kind happen to be when subjected to the rays. The idea that the rays have a selective property, so well understood by medical radiologists but so unintelligible to those who are not familiar with radiologic physics, was first enounced by Regaud and has since been widely accepted as meaning that rays (radium or roentgen rays) of a certain range of wave length may induce marked pathologic changes in deep tissues or tumors without any or with much less effect on the overlying or intervening superficial tissues.

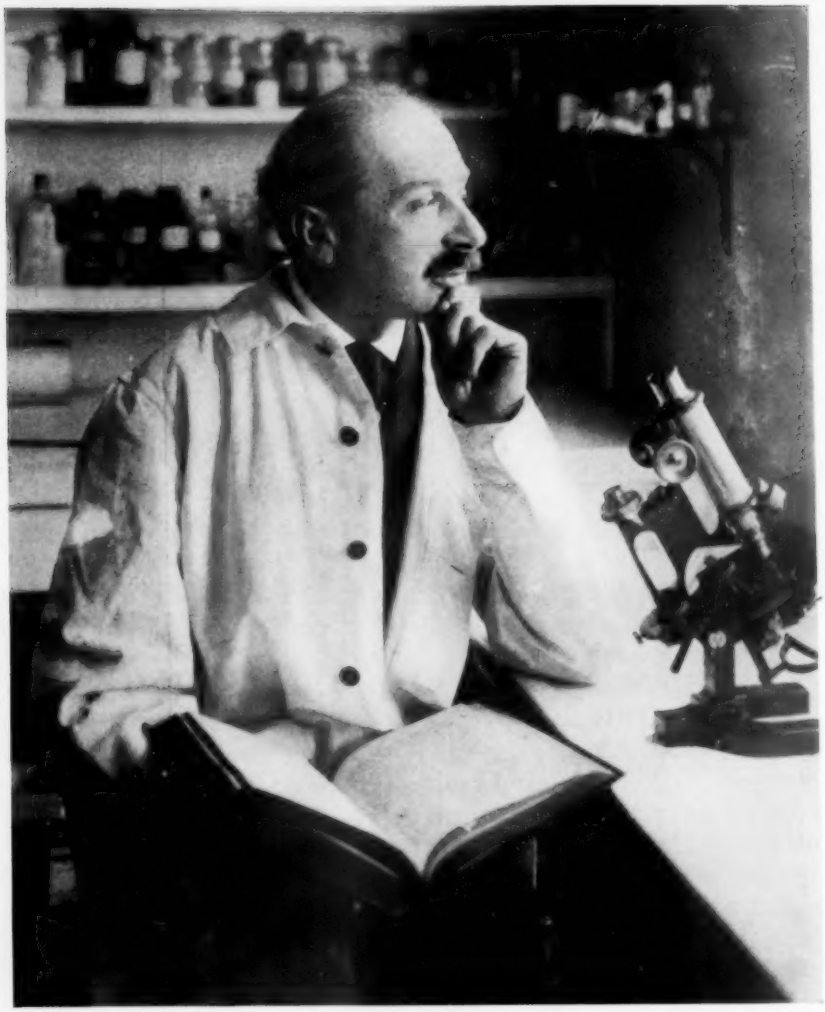
Could the death of cells after irradiation be accounted for only by vascular changes such as Pullinger has described, how could the characteristic and specific difference in the radiosensitiveness of different varieties of cells be explained? For example, why should the lymphocytes be so extremely sensitive to the rays and the nerve cells so extremely resistant? If interference with circulation were the primary, direct and indispensable factor in the death of cells, one might infer that all cells, whatever

their variety, should be injured or damaged at approximately the same rate. At least, any difference in the influence of vasodilatation, hyperemia, thrombosis, extravasation of blood and separation of serum should influence all cells in the affected area to a greater or smaller degree according to the extent of the circulatory factors, irrespective of the variety of the cells. And yet, more careful consideration shows that even the property of specific radiosensitiveness of different kinds of cells might perhaps be consistent with the destruction of cells by vascular changes. It must be apparent that cells deprived of nourishment must degenerate and that the rate of degeneration of different kinds of cells may be related to their metabolic activity or status. In other words, even the peculiarly significant relation of metabolic activity (rate of mitosis) to radiosensitiveness need not necessarily invalidate the idea of vascular alterations as the primary cause of cell death, were it not for one thing. If the vascular changes, to which Pullinger attributes the death of all cells after exposure to radium or roentgen rays, were a primary and direct result of irradiation, they must be due to action of the rays on the cellular components of the vessel walls, on the blood corpuscles and platelets, or on both. The endothelial cells lining the blood vessels have often been shown to be injured or destroyed by radiation, but only by doses of the order of those required to induce inflammatory reaction in the irradiated tissues. Smaller doses do not have any perceptible effect on vascular endothelium. A direct effect on the endothelial cells or on the cells of the media, therefore, can hardly be invoked. Moreover, the exceptional resistance of nerve cells to radiation does not allow one to think that the primary action of the rays affects the vasomotor nerve fibers. Consequently, the only alternative is for the vasodilatation and hyperemia to be secondary to the influence of the rays on other more sensitive cells in the exposed territory or on the leucocytes in the circulating blood.

As far as the blood corpuscles are concerned, it has long been established that the lymphocytes are the most radiosensitive of all cells. In this respect their susceptibility is the same, whether they are circulating in the blood, in the sinuses of the spleen, lymph nodes, intestinal follicles, or bone marrow, or whether they populate the lobules of the thymus gland. The polymorphonuclear neutrophile and eosinophile cells are distinctly less vulnerable, and the erythrocytes much less. In the salivary glands, in the bronchi and trachea, and in the intestine also, epithelial cells that have the property of secreting mucus are much more susceptible to irradiation than other epithelial cells that do not secrete mucus. If the death of cells must result from vascular disturbances leading to circulatory impairment, it would seem rather strange that certain cells in a given layer of closely related cells should suffer so much more from the same dose of radiation than other cells in the same circulatory environment.

Considerations such as these and many others which might be cited are difficult to reconcile with the hypothesis advanced by Pullinger. Analysis of the extensive experimental evidence on the action of radium and roentgen rays indicates that the rays act primarily on the most sensitive cells in the irradiated area, that the degree or rapidity of the radiation effect varies with the dose of rays, the age of the animal or human being, the metabolic activity of the cells as represented by their life cycle, and the stage of mitosis in which the cells happen to be at the time of exposure. The dogma that pathologic cells are more radiosensitive than normal cells of the same kind is valid only to the extent that their rate of metabolism or mitosis may be increased by the pathologic disturbance and applies, therefore, only to tumors and pathologic processes of which cellular hyperplasia is an important element.

A. U. Desjardins



EMIL G. BECK
1866-1932

IN THE death of Emil G. Beck on July 1, at the age of sixty-six, the American Roentgen Ray Society mourns the loss of a member who has contributed in an important way to the advancement of the science of roentgenology. The genial disposition and keen wit of this talented investigator endeared him to his numerous friends.

Born in Czechoslovakia, Dr. Beck received his early education in Prague and at the age of twenty came to this country to settle in Chicago where he subsequently achieved international fame as a surgeon. In his early days, Dr. Beck was associated with a Chicago manufacturing enterprise, but later worked his way through the Medical School of the University of Illinois from which he was graduated with honors in 1896. In 1901 he engaged in graduate work in chemistry and surgery at Berlin and Zurich.

In 1904 he began his work in radiology, experimenting at first with the demonstration of sinus tracts by means of an opaque paste consisting of a combination of bismuth and vaseline of a proper melting point,

which came to be known as "Beck's paste." It was soon ascertained that in certain cases of tuberculous fistulae and abscesses the introduction of the paste had a beneficial effect and the method became widely used both for diagnosis and treatment until the later development of the iodized oil preparations which are now so popular. In 1908 Dr. Beck devised a method of sliding skin grafts for lining empyema cavities, and for the treatment of osteomyelitis in favorable cases. Later another contribution was the open method of treating advanced cancer with roentgen radiation administered during the operation or shortly after the termination of the surgical procedure. For this later work Dr. Beck received the gold medal of the Radiological Society of North America in 1923. Long before, in 1908, the American Medical Association had awarded him a certificate of honor for his research work in carcinoma.

Dr. Beck was always interested in photography, especially stereoscopic photography in colors. Those of us who had the privilege of visiting his clinic were often treated to very instructive and attractive demonstrations of the numerous stereoscopic photographs, many in colors, and in the stereoscopic roentgenograms for which he was deservedly famous. Most of us possess a copy of his stereoscopic atlas on foreign bodies, a comprehensive treatise on the localization and removal of foreign bodies, with special reference to the thorax.

With his brothers, Carl (engaged in general surgery) and Joseph (specializing in oto-laryngology, and author of an excellent early atlas of roentgenography of the mastoids and facial sinuses), Dr. Beck, known to hundreds of grateful patients in his home city as "Dr. Emil," built and maintained the North Chicago Hospital.

Aside from his professional accomplishments which raised him to a high place in the medical world, Dr. Beck achieved recognition as a peace exponent and for his philanthropies. When the Bok Peace Prize was offered to the world, Dr. Beck drafted a pamphlet entitled "Reciprocal Representation in the World Assembly," which was decreed of such value that it was officially laid before The Hague Conference, and also brought him praise from world leaders in the peace movement. A later revision of his plan has been in the hands of the Committee on Peace Plans at Washington, D.C.

In addition to the American Roentgen Ray Society, Dr. Beck was a member of many scientific societies, including the county, state and national societies to which most physicians belong, the National Tuberculosis Association, the Radiological Society of North America, the Western Surgical Association, the Chicago Surgical Society, the American Society for Thoracic Surgery, the American College of Surgeons and others. Dr. and Mrs. Beck were always to be found at the important national conventions of medical societies and at many of the international meetings held in this country and abroad.

The last few years of Dr. Beck's life were spent in Berkeley, California, where he was on the staff of the Merritt Hospital. He is survived by his widow, Mrs. Clara Hyde Beck, a daughter and two grandchildren, and two brothers, Dr. Joseph and Dr. Carl Beck.

James T. Case

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Annual Meeting: Detroit, Mich., Sept. 27–30, 1932.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: Milwaukee, Wis., 1933.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio.
Annual meeting: Milwaukee, Wis., 1933.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y.
Annual Meeting: Atlantic City, N. J., Nov. 28–Dec. 2, 1932.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, Dr. D. R. MacColl, 2826 S. Hope St., Los Angeles, Calif.
Meets on the third Wednesday of each month at the California Hospital.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. C. H. Heacock, 20 S. Dunlap St., Memphis, Tenn.
Annual meeting: Birmingham, Ala., Nov. 16–18, 1932.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. J. J. Masterson, 401-76th St., Brooklyn, N. Y.
Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y.
Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. H. G. Reineke, Christian R. Holmes Hospital, Cincinnati, Ohio.
Meetings held monthly.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. M. A. Thomas, Medical Arts Bldg.
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. W. McL. Shaw, 418 St. James Bldg., Jacksonville, Fla.
Meetings held twice a year, May and November.
Next meeting, Jacksonville, November, 1932.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. L. M. Hilt, Myers Bldg., Springfield, Ill.
Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee, Wis.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.
Next meeting, Duluth, Minn., Oct. 8, 1932.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. J. Bennett Edwards, Englewood Hospital, Englewood, N. J.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. M. T. Powers, 250 Genesee St., Utica, N. Y.
Three meetings a year—January, May and November.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Next Meeting: Philipsburg, Pa., May 18–19, 1932.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thomson Hall, College of Physicians, 19 S. 22d St.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

ST. LOUIS ROENTGEN CLUB
Secretary, Dr. W. K. Mueller, University Club Bldg.
Meets first week of each month. Time and place of meetings designated by president.

TEXAS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

UNIVERSITY OF MICHIGAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Wednesday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Meets annually in October.
Next meeting: Richmond, Va., October, 1932.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Allies, 134, Louvain, (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd-und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Maracine 30, Bucarest, Rumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Secretary, Professor Holzknecht, Vienna, IX, General Hospital.
Meets first Tuesday each month, October to July.

Orient

Japan X-ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike, Kyoto, Japan. Meets bi-monthly on third Sunday.

SOCIETY OF THE GERMAN ROENTGENOLOGISTS AND RADIOLOGISTS IN THE REPUBLIC OF CZECHOSLOVAKIA*

The Ninth Meeting of the Society of German Roentgenologists and Radiologists in the Republic of Czechoslovakia was held in Prague, November 7 and 8, 1931, under the presidency of Jaksch-Wartenhorst and with Altschul as secretary, and was well attended by radiologists both from Czechoslovakia and abroad. The president gave an address in memory of the honorary member, Martin Haudek, and a charter member and treasurer of the society, Fritz Porges. The address for the deceased honorary member, Guido Holzknecht, was given by his pupil Herrnheiser.

I. *Indications for Roentgen Therapy in Skin Diseases*

Brünauer of Vienna discussed in detail the indications and contraindications for roentgen treatment of diseases of the skin, including the irradiation of inflammatory lesions, the different forms of indirect irradiation and the therapy of benign and malignant skin tumors. Numerous excellent lantern slides illustrated this lecture.

Schoenhof, Prague, discussed the technique of irradiation in skin therapy, devoting special attention to the determination of the field of radiation and of the uniform distribution of roentgen rays within a certain field. He also discussed the determination of the radiation quality and its relation to the depth of the lesion and emphasized the importance of the exact determination of the dosage used.

In the discussion, Ghon of Prague called attention to the importance of considering the stage of tumor growth in radiation therapy, and inquired about the position of radiation therapy in recurrent forms of eczema. Brünauer answered that the same statement holds for recurrent forms as for other types. Samek of Prague discussed the position which the Prague German Skin Clinic takes in regard to the three groups of positive indication, relative indication and contraindication.

Lectures on Therapy. Samek, Prague, illustrated the roentgen-ray damage in the irradiation of dermatoses and suggested avoiding them by refusing to use any set scheme in treatment, and by further separation of the application of the single dose.

Schliephake, Jena, reported on the treatment of purulent diseases with short electric waves. Such treatments were very successful on abscesses produced artificially in animals as well as on inflammatory diseases in man.

Steiner, Teplitz, gave a report on the successful treatment by irradiation of two cases of malignant goiter and warned against painting the neck with iodine since this prevents or delays the effects of irradiation.

Bardachzi and Epstein of Aussig, reported on their preliminary experiences with the method of protracted and fractional irradiation according to Coutard with which they did not obtain any better results than with the ordinary doses. In the discussion Schinz spoke on his experiences at the Zurich Clinic. He could not support the point of view of these investigators and believed that the failure of definite results in their experiments could be explained by the fact that their total dosage was too small. Bardachzi in his conclusion answered that his cases belonged to another group of indications, since their experiments were intended to work out the method for the cases treated in the department of clinical medicine.

Radium Therapy. Markl, Joachimsthal, made experiments on the amount of energy which acts upon the tissue in a radium bath, and found that the threshold value of the biologic effect can be reached.

Altschul, Prague, described excellent results in cases of rheumatism of the muscles and joints, arthritis, neuralgia, and similar diseases, treated with a series of injections of weak solutions of radium chloride.

* Translated from the German by Otto Glasser, Ph.D., Cleveland Clinic, Cleveland, Ohio.

(Ampules—"Radiumchema," 1 and 2 microcurie.)

Schloss, Vienna, described a method of irradiation of the vessels with radium in disturbances of the circulation. In 77 per cent of the cases he obtained completely successful results.

II. *Borderline between Normal and Beginning Pathologic Conditions in Bones as Seen in the Roentgenogram*

Schinz, Zurich, discussed the difficulty of deciding what is normal and what is pathologic in roentgenograms of bones. Such difficulties can be caused by roentgenologic errors, and often phylogenetic remainders, individual idiosyncrasies and genotypical variations are misinterpreted as pathologic conditions. It is not always possible to find the beginning of disease, for instance, in osteomyelitis. On the other hand, severe bone changes may be found in patients who are free from clinical symptoms. The change from pathologic to normal can often cause mistakes in the diagnosis, which is of great importance in deciding questions in insurance medicine.

Altschul, Prague, limited his remarks to the discussion of external influences which cause pathologic changes definitely present not to be visible on the roentgenogram. He illustrated this by showing roentgenograms of the living and of anatomical preparations. Such influences include poor technique, which does not produce perfect pictures; the direction of the roentgen beam since certain changes can be made visible only for one certain direction; false interpretation due to special projections; and state of the disease or youth of the patient which possibly prevent the visibility of changes. He called attention to the importance of a control roentgenogram of the normal side which is often the only means of making a correct diagnosis.

Löw-Beer, Prague, discussed several phases of cranial roentgenology which showed the difficulty of recognizing the correct borderline between normal and pathologic conditions.

In the discussion, Steiner demonstrated two cases of post-traumatic navicular cysts. Reiser, Prague, demonstrated roentgenograms of fissures which could be made visible only after atypical roentgenograms were made. He showed, in addition, two cases in which there were increased areas in relief in the roentgenogram of the skull without the presence of an obstructing papilla. Finally, he showed a calcification between the two vertebrae which was diagnosed as a calcification of the nucleus pulposus. Discussing the paper of Löw-Beer, Steiner of Teplitz called attention to the difficulty of correct diagnosis at the boundary lines of the accessory sinuses. Kraus, Prague, discussed the frequent mistaken diagnoses of hypophyseal tumors, if the sella is enlarged by cerebral pressure. He illustrated this from a wealth of material on cerebral tumors.

Bone Pathology. Ghon, Prague, demonstrated a case in which the differential diagnosis between bone tumor and localized fibrous osteitis could not be made either from a roentgenologic or histologic point of view.

Reimann and Salus, Prague, reported on lymphogranulomatosis of the bone. The morphologic picture in the roentgenogram is so varied that it is hard to make a definite diagnosis.

Herrnheiser, Prague, spoke on the roentgen diagnosis of the bony orbit. It is possible to diagnose hyperostosis and processes of destruction, changes in the sinuses, traumatic changes and anomalies in dimensions.

Meller and Gottlieb, Bucharest, demonstrated a congenital malformation of the cervical spine (torticollis).

Kuh, Prague, gave a report on a congenital defect of the fibula with changes in the ankle. Reimann, Prague, reported two cases of meningocele.

Weil, Prague, reported on isolated gummatous processes of the scapula and M. Klein, Prague, spoke on the experiences in the German Children's Hospital with 158 cases of congenital luetic bone affections

of the hand, using numerous roentgenograms in his discussion.

L. Pokorny, Komotau, showed roentgenograms from a case of osteitis deformans (Paget); Sanlader, Troppau, a picture of a case of angioma ossificans of the eighth rib; Jaroschy, Prague, an asymmetrically atrophic pelvis with protrusion after an injury and an osteomalacic pelvis due to neglected rachitis; and Mendl, Brunn, the roentgenograms of the temporal bone of a patient with osteopsathyrosis idopathica.

Salus and Reimann, Prague, reported two cases of generalized joint osteomatosis (Kienböck) on a tabetic basis. In the discussion Jaroschy and Mittelbach rejected the new name, osteomatosis.

Herzog, Witkowitz, demonstrated several cases of juvenile osteochondritis of the thigh. Hilgenreiner, Prague, who introduced the name of this disease in a previous publication found in these cases a support of his previous opinions, especially in relation to the endocrine dysfunction.

Epstein, Aussig, demonstrated a case of spondylolisthesis of the fourth lumbar vertebra. Jaroschy, Prague, also showed a case of spondylolisthesis, but stated that he does not believe in a traumatic etiology of this condition.

Altschul of Prague, and Schiller of Wlaschim gave their experience with tuberculosis of the vertebrae and discussed the different forms which can be shown in roentgenograms. The disease usually attacks the lowest part of the dorsal spine and the upper lumbar vertebrae. In the discussion Koppenstein, Budapest, called attention to the importance of the technique of examination and recommended the Bársony-Koppenstein position.

Thorax. Gütig, Witkowitz, reported on the removal of a needle which had wandered within thirty-six hours through the wall of the thorax into the heart. Meller, Bucharest, reported on a case of transposition of the great vessels in which he made an artificial circulation of the contrast meal and elucidated the pathologic conditions by means of roentgen examination.

Mannl, Karlsbad, demonstrated a case of total situs inversus.

Abdomen. Gütig, Witkowitz, demonstrated one case of megabulbus, and one of megaduodenum in luetic patients.

Mannl, Karlsbad, showed a case in which the fundus of the bladder could be pushed into the body by a contraction of the diaphragm.

Schütze, Berlin, reported on a peculiar case of duodenal carcinoma which started from the papilla Vateri, and spread into the stomach like a foreign body. He furthermore demonstrated a large diverticulum of the stomach at the upper portion of the small curvature. Koppenstein, Budapest, demonstrated four cases of diverticulum at the cardiac end of the stomach. He also showed two cases of postoperative jejunal ulcer.

Herz, Berlin, discussed roentgenologic changes after the ordinary operations for the treatment of perforated ulcers of the stomach and duodenum.

Steiner, Teplitz, reported on roentgenologic studies of the mucous membrane of the esophagus and showed several roentgenograms.

Meller, Bucharest, reported on a new method of examination of the relief area of the mucous membranes of the stomach by means of a caustic. He used colloidal aluminum and umbrathor.

Fleischner, Vienna, reported on a stenosis of the large intestine as a result of extracolic processes. From a roentgenologic point of view, such adjoining processes can be separated by the presence of the mucous membrane.

Epstein, Aussig, demonstrated cases of ulcerative colitis and called attention to the importance of the relief presentation.

Beutel, Prague, reported on his experiences with hepato-lienography. This method is contraindicated in diseases due to hypersensitivity.

Gütig and Herzog, of Witkowitz, demonstrated numerous roentgenograms for the diagnosis of kidney diseases and called

attention to the importance of complete roentgenograms from the kidney to the bladder and they warned against overemphasizing or underemphasizing the value of intravenous urography.

Technique. Franke, Hamburg, reported on studies on the change of the character of the roentgenogram of the lungs due to a change in radiation quality. The automatic exposure apparatus proved very valuable in these experiments. In the discussion, Adler recommended keeping the medium hard technique.

Meyer, Berlin, spoke on the modern construction of the mekapion and demonstrated the principle of the durometer.

Graf, Berlin, reported on the tuto cover which combines small dimensions with a complete protection against roentgen rays. He also described a new type of roentgen apparatus for superficial therapy which contains a stabilizer for line fluctuations. In the discussion, Schoenhof warned against too much simplification of the rather complicated superficial radiation therapy.

Mannl, Karlsbad, demonstrated an adjusting device for roentgenograms in which an auxiliary light is reflected by a mirror in such a way that it seems to come from the target.

W. Altschul

SPECIAL RAILROAD RATES

All members and guests who anticipate attending the Detroit Meeting of the American Roentgen Ray Society in September are requested to purchase one-way tickets and ask for Convention certificate at that time. If one hundred certificates are presented, return tickets may be purchased at one half of the regular one-way fare.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

A Text-book of X-Ray Therapeutics. By Robert Knox, M.D., C.M., Edin.; M.R.C.S., Eng.; L.R.C.P., Lond.; M.I.E.E., D.M.R.E. Completed and edited by Walter M. Levitt, M.B. Irel.; M.R.C.P., Lond.; D.M.R.E., Camb., Medical Officer in Charge of the Radiotherapeutic Research Department and Assistant Medical Officer to the X-Ray Department, St. Bartholomew's Hospital, London. Fourth Edition. Cloth. Price, $7.00. Pp. 250, with 11 full page plates and 95 illustrations in the text. New York: The Macmillan Company; London: A & C. Black, Limited, 1932.

As stated in the prefaces, this book is an attempt to complete a work on radiotherapeutics which Dr. Knox had in course of preparation at the time of his death.

It was considered necessary to change Dr. Knox' original plan and limit the subject matter to roentgen-ray therapeutics. This is regrettable because the subjects of roentgen therapy and radium therapy cannot be dealt with separately in a very satisfactory manner. The book, therefore, reflects the insuperable difficulties under which it was written.

Following a brief introduction there is a chapter devoted to the effects of roentgen rays upon tissues. Then follow several chapters which are devoted to physics, measurements, filters, apparatus and therapeutic technique. The last half of the book deals with the use of roentgen rays in various diseases. There are also two appendices one of which is devoted to a paper read by Dr. Knox at the Second International Congress of Radiology, Stockholm, which, though excellent for such an occasion, seems out of place in a textbook.

The physical and technical aspects of roentgen therapy are very well covered. Dosages are expressed by a biological unit designated as "unit skin dose." A conversion table into international r units is given. It will appear odd to American readers that the term "roentgen" is nowhere used.

In discussing malignant neoplastic diseases one is struck by the ultraconservative claims for radiotherapy. As an example may be cited a statement in regard to treatment of epithelioma of the lip that "neither radium nor x-rays alone should be relied upon if the case is at all operable." With this, and other similar statements, many radiotherapists will not agree.

A chapter is devoted to a discussion of seventeen non-malignant dermatological conditions. It will seem strange to many that a page should be devoted to hypertrichosis, and that such common maladies as boils and carbuncles should go unmentioned. To others it will seem equally odd that in discussing diseases of the chest more than a page is devoted to the roentgen treatment of pulmonary tuberculosis and that the value of such treatment in unresolved plenumonia is not referred to.

It is somewhat disconcerting to the reader to come across statements in the text that seem contradictory, but notwithstanding what may be regarded as faults both of omission and commission he will find the book, as a whole, to be highly instructive. It is, therefore, unhesitatingly commended to the attention of those having a sufficient knowledge of the subject to enable them to exercise proper discrimination.

The book is well printed and amply illustrated.

Thomas A. Groover

Electrosurgery. By Howard A. Kelly, M.D., LL.D., F.A.C.S., Baltimore, Maryland, and Grant E. Ward, M.D., F.A.C.S., Baltimore, Maryland. Cloth. Price, $7.00. Pp. 305, with 382 illustrations. Philadelphia and London: W. B. Saunders Company, 1932.

Although high frequency currents have been used rather extensively for some twenty years by those radiologists interested in the treatment of cancer, this book brings the method forward as a new surgical procedure and to most surgeons it is, no doubt, quite new. Electrosurgery has, during the past few years, crept into almost every surgical specialty and it is indeed fortunate that two men of such outstanding ability have seen fit to gather all of the better techniques into one volume which is an authoritative reference book.

A short chapter deals with the underlying

electrical principles and wiring diagrams of apparatus. Since most medically trained minds will find this material wholly unintelligible its brevity is perhaps excusable, but a description of the control boards explaining how they are used in practice would have been of great value to the beginner. The three standard procedures, namely, electrodesiccation, electrocoagulation and acusection are described in some detail and numerous histological studies of their effects on living tissue are included. Proper emphasis is placed on the ease with which hemostasis may be obtained without ligatures and the efficient closure of lymphatics that follows coagulation. Attention is called to the excessive cost of the apparatus now available and a plea is made for more investigation leading to better equipment.

Separate chapters are devoted to the skin, oral cavity, oto-laryngology, thyroid, thorax, breast, abdomen, gynecology, urology, proctology, and the central nervous system. Other workers in this field are frequently referred to. The chapter on the thorax is written by Thomas Bayson Aycock and the one on bladder tumors by Hugh H. Young, while Harvey Cushing is quoted freely in the section dealing with intracranial disease. So many operations are described that they cannot even be enumerated here. One is struck with the fact that in many instances the electrical procedure is easier on the patient than the older surgical methods, and its superiority in the treatment of malignancy is made evident. The desirability of using roentgen and radium therapy along with electrosurgery is mentioned repeatedly throughout the book and the final chapter is entitled "Irradiation and Electrosurgery."

All technical procedures are described with great attention to detail and an abundance of illustrations of excellent quality amplify the text. The most important facts gleaned from the book are (1) that electrosurgery makes certain operations possible that could not be attempted without it, and (2) that some cases of carcinoma looked upon as hopeless and inoperable may, with the aid of electro surgery and irradiation, be given a more hopeful outlook.

Charles L. Martin

The Heart Rate. By Ernst P. Boas, M.D., Associate Physician, Mt. Sinai Hospital, New York City, and Ernst F. Goldschmidt, Ph.D., Research Fellow (1930–1931), Department of Surgery in the Yale University School of Medicine. Cloth. Price, $3.50. Pp. 166, with 68 illustrations. Springfield, Illinois: Charles C. Thomas, 1932.

An original and brilliant investigation of the heart rate, with total counts of the apex beat over prolonged periods of time, has been achieved by Boas and Goldschmidt. The instrument used in this investigation, known as a cardiotachometer, is based on the principle of the amplification of the action currents of the heart. The current is led off by means of two electrodes placed over the anterior aspect of the chest in such a manner as to obtain maximum voltage response. A 4-tube transformer coupled amplifier, possessing the characteristic of high gain at low frequencies, is used to amplify this current (the R-wave of the electrocardiogram). The amplified signal is fed into a system of relays which actuates an electromagnetic counter and graphic registering device. The counter records accurately total number of cardiac cycles over periods of twelve to twenty-four hours.

While the heart rate has been studied intensively for several hundred years, the writers have invaded a practically original field in accurately recording rates and total counts of the heart under varied physiological and pathological conditions. Observations are included on the minimum, maximum, and average rates during the waking state and during sleep, with interesting and, in many instances, new correlations between these various rates. The flexibility of the apparatus permitted a study of the rate in relation to (*a*) various forms of exercise such as dancing, simple forms of work, and exhausting fatigue; (*b*) diverse normal physiological conditions; (*c*) anesthesia and operations, as well as (*d*) pathological conditions relating to the heart.

The work during sleep was particularly painstakingly done, and the investigators have been well rewarded for their efforts.

The work is profusely illustrated by means of graphs, which show at a glance the variations in the heart rate during the experiments. At the end of the monograph there is an appendix with tables summarizing much of the work, and a good bibliography.

The work is of great importance from the physiological standpoint. The roentgenologist in his study of the heart will find many ways in which the knowledge incorporated in this monograph can be profitably applied to his field; particularly in regard to his fluoroscopic observations.

Walter W. Fray

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN AND RADIUM THERAPY

DORNE, MAURICE, and WHITE, CLEVELAND. Treatment of superficial fungus infections with the long wave length roentgen rays (Grenz rays). *Arch. Dermat. & Syph.*, Sept., 1931, *24*, 409–416.

This study was pursued for the purpose of evaluating the therapeutic possibilities of the so-called grenz rays. The literature is briefly reviewed, and the long wave roentgen ray compared and contrasted to the short wave roentgen ray.

A special generator was used delivering a maximum of 12 kv. and 12 ma. to a specially constructed Coolidge tube with the Lindemann glass window on the under surface of the tube. The erythema dose of this apparatus was 8 kv., 6 ma., 3 in. distance, 1 min. Erythema appeared within twenty-four hours. A fractional method of treatment was used: one-fourth erythema dose was given at weekly intervals for four treatments. In those cases in which large areas were treated requiring repeated focusing, the dosage was reduced one-half; in treatment of the nails the dose was doubled. In several instances where recurrences occurred one or two additional treatments were given.

A summary is given of 30 cases thus treated. Routine smears stained with potassium hydroxide, and cultures (Sabouraud's dextrose medium) were taken. All patients were followed for a sufficiently long period apparently to determine the clinical value of the grenz ray. By use of fractional doses of long wave length roentgen rays (grenz rays) good results were obtained in patients who had infections due to yeast-like fungi, while the infections of hyphomycetic origin showed very little, if any, im-

provement. This series is only sufficiently large to give suggestive, no conclusive, results.—*Ellsworth Johnson.*

Dean, Archie L., Jr., and Quimby, Edith H. Radiation therapy of carcinoma of the bladder. *Surg., Gynec. & Obst.*, July, 1931, *53*, 89–96.

This paper describes the methods of treating cancer of the bladder at the Memorial Hospital, analyses the radiation furnished by the use of radium and roentgen rays and presents the results following radiation therapy in contrast to surgery alone.

If the base of a papillary carcinoma is no larger than 1.5 cm. in diameter and is entirely visible through the cystoscope, the tumor may be treated successfully with gold radon seeds implanted through the urethra. Larger papillary cancers and all infiltrating tumors necessitate a suprapubic cystostomy. The bladder is never separated from its attachments and resection is never done. Intravesicle tumor projections are removed with the actual cautery or endotherm knife. The base is not coagulated. Gold radon seeds of 2 mc. each are buried 1 cm. apart and 1 cm. deep and 1 cm. beyond any evidence of involvement.

Tables are presented which indicate the tissue dose of radiation delivered. The minimum tissue dose used was found to be between 20 and 25 threshold erythema doses. Large doses of interstitial radiation are used because the inaccessibility of the bladder demands a single curative dose. Careful estimates show that 1.2 threshold erythema doses is about as large a dose as can reach a bladder tumor from a single pelvic cycle of four high voltage roentgen treatments.

In a series of 51 cases of papillary carcinoma with histological diagnosis and a series of 45 cases with a clinical diagnosis, between 43 and 55 per cent of the patients are free from symtoms and signs of disease three years after treatment.

In a series of 44 cases of infiltrating carcinoma with histological diagnosis and a series of 82 cases with a clinical diagnosis, between 27.8 and 31.8 per cent of the patients are free from symptoms and signs of disease three years after treatment.

The operative mortality is less than that from surgery alone in proportion of 3.7 per cent compared with 10 to 20 per cent.

The authors believe from their experience with radium therapy as it is employed at the Memorial Hospital that adequate interstitial irradiation is preferable to surgery alone in the treatment of both papillary and infiltrating types of bladder cancer because the operative mortality is less, and a higher percentage of patients are free from disease three years after treatment.—*R. R. Rathbone.*

Cutler, Max. The treatment of mammary carcinoma by means of removable radium needles. *Surg., Gynec. & Obst.*, July, 1931, *53*, 71–76.

The author describes in detail his method of treating inoperable carcinoma of the breast by interstitial radiation. Some of the difficulties encountered in such treatment are discussed. Keynes' method of interstitial radiation is reviewed, as well as Cheatle's.

Two case reports are given showing the satisfactory primary regression of the tumor. Stainless steel needles, 9, 6, and 3.5 cm. in length are used, holding gold and glass radon tubes having a total filtration equivalent to 0.5 mm. platinum. The millicurie value of each needle is approximately 1 millicurie per centimeter of length. Under local anesthetic the needles are introduced through puncture wounds previously made by a scalpel. To the needles are attached thin steel wires by which they are withdrawn after seven to nine days.

In placing the needles, the main mass of the tumor is avoided, the periphery of the growth being the objective. This lessens the danger of dissemination of the tumor cells by trauma and prevents over-irradiation of the tumor. The axillary, supraclavicular, and intercostal regions are irradiated in every case, however localized the breast disease appears. The number of needles depends upon the size of the breast, as they are spaced approximately 1 cm. apart. The interstitial radiation is supplemented by external radium packs.

Healing of ulcerated lesions of the breast can be accomplished and impending ulceration prevented by such treatment. As yet no claim can be made for the permanency of results.—*R. R. Rathbone.*

Spiethoff, B. Die Behandlung des Lupus vulgaris mit Grenzstrahlen. (The treatment of lupus vulgaris with Grenz rays.) *Strahlentherapie*, 1931, *40*, 245–255.

Grenz rays make possible prolonged treat-

ments and increase of dose up to the desired reaction without danger of irreparable damage. The treatment factors used in the Jena Dermatological Clinic are 9 kv.; 10 ma.; and 2.5 cm. distance (window-skin). For these conditions a dose of 4,600 r was obtained in 2 minutes and 20 seconds from a Müller Grenz-ray tube. Lupus vulgaris has been very successfully treated with Grenz rays. The dose for average infiltration was 4,600 r. For hypertrophic or verrucous lesions higher doses were applied which range from 11,000–22,000 r. These doses were repeated after the irradiation reaction had disappeared.—*Otto Glasser.*

SCHILLER, VIKTOR, and ALTSCHUL, WALTER. Welche Rolle spielt die Röntgenbestrahlung bei der Behandlung der chirurgischen Tuberkulose? (Roentgen irradiation in the treatment of surgical tuberculosis.) *Strahlentherapie*, 1931, *41*, 755–761.

The authors come to the conclusion from their work in a tuberculosis sanatorium that roentgen irradiation is indispensable in the treatment of surgical tuberculosis in combination with other methods of treatment, but the results depend on close cooperation with the clinician. Ambulant treatment should not be given except in inactive cases, as the reaction of the patient to the irradiation must be watched closely in active cases. There is no reaction in inactive cases and if no reaction is seen on repeated examinations it proves that the process has become inactive. Active cases show rise of temperature, general weakness and loss of appetite. Locally there is swelling at the focus, increased secretion and pain. As a rule, these symptoms pass off in two to three days. Febrile cases with secondary infection are absolutely intolerant to even the smallest doses. General directions as to dosage cannot be given. The beginning doses should be very small and the further course of the treatment determined by the patient's reaction. The fresher and more florid the process, the smaller the beginning dose should be.

The authors have had excellent results in lymph gland tuberculosis, scrofuloderma, infiltration of the epididymis and also in closed caries of the ribs. Gravity abscesses heal under roentgen treatment following evacuation and iodoform glycerin. Of course the primary focus is irradiated also. It often requires some months' treatment to affect bone processes. Irradiation seems to have a tendency to prevent ankylosis of joints, which is important in cases that have to be immobilized a long time.—*Audrey G. Morgan.*

SOUTTAR, H. S. Radium in the service of surgery. *Brit. M. J.*, Jan. 3, 1931, *1*, 1–5.

Breast.—The author recommends the introduction of radium seeds into tumors of the breast, into accessible metastases and in the paths of lymph drainage.

Tongue.—The author states that there can be no question that in the tongue, radium is the treatment of choice. He advocates the use of radium seeds introduced interstitially in the tongue and into the neck if the lesion is advanced. In cancer of the *lip*, from which secondaries only arise at a late stage, a permanent cure of an early case is so certain that the glands may be ignored.

Rectum.—The rectum is a region peculiarly adapted to the use of seeds, whether the growth is within reach of the anus or can only be reached from the abdomen. Carcinoma of the rectum is very sensitive to radium.

Cervix cancers respond with extreme readiness to treatment with radium.

The author, a surgeon, discusses the physics and biological effects of radium.—*J. H. Vastine.*

DALE, T. Eine neue Methode der Röntgenbehandlung von Leukämie. (A new method of roentgen treatment of leucemia.) *Acta radiol.*, 1931, *12*, 263–286.

The author describes a new method of roentgen treatment of leucemia which he has used for the past two years. It consists of general irradiation of the body from a distance of 1 meter; filter 0.5 mm. zinc. The head, neck and genitals are screened during the exposure. Irradiations of 12 to 18 minutes daily were given for a period varying from 4–5 days to 5 weeks to a series. A total of 1/10 to 4/5 of a skin erythema dose was given to a series.

Four cases of myelogenous leucemia were treated in which local irradiations of the spleen had been given previously. In these cases, in which the local treatment of the spleen had been ineffective, temporary improvement was obtained.

Four other cases of myelogenous leucemia were given general irradiation only. Two of these patients remained able to work for the two years during which the treatment was continued. Two cases of lymphatic leucemia were given general irradiation only. One of the pa-

tients remained able to work for twenty-one months. The author maintains that general irradiation is superior to the local irradiation that has been in use heretofore because it is less severe and enables the patient to keep up his work for a longer time. Unlike Teschendorf, the author, though he used much larger doses, never saw any general reaction from the treatment.—*Audrey G. Morgan.*

Hoffman, William J., and Craver, Lloyd F. Chronic myelogenous leukemia; value of irradiation and its effect on the duration of life. *J. Am. M. Ass.*, Sept. 19, 1931, *97*, 836–840.

Eighty-two cases of myelogenous leucemia are analyzed and compared with the series reported by Minot, Buckman and Isaacs. The duration of symptoms before diagnosis varied from one month to twelve years, the group average being 0.75 years. Splenomegaly was present at the time of diagnosis in 77 of the 82 cases. The duration of life varied from six months to over sixteen years. Irradiation apparently adds little to the duration of life, this being the same whether or not both spleen and long bones were treated. The duration of efficient life is, however, definitely increased by irradiation, since the steady decline of the untreated cases is replaced by remissions in which comparative health follows irradiation.

The authors' technique consists of giving about one-sixth of an erythema dose over the spleen on four to six successive days.—*E. W. Hall.*

Werner, R. Über den gegenwärtigen Stand der Radiumtherapie. (Present status of radium therapy.) *Strahlentherapie*, 1931, *41*, 727–745.

The different methods of application of radium are reviewed. In skin diseases superficial irradiations with weak filtration are often used and sometimes radioactive salves, which generally contain thorium X. The dermatological indications for radium treatment are about the same as for roentgen treatment. In sensitive efflorescences the irradiation must be very mild. In superficial angiomas the cosmetic effect is better, the slower and more carefully the treatment is carried out. Cavernomas should be emptied by compression so that the rays may act more intensely on the endothelial cells. The same is true of lymphangiomas which react very well to radium treatment. Keloids must be irradiated more intensely but it is better to divide the dosage. The cosmetic results are better with the slower method. The different forms of nevi react well to radium treatment and pigmented nevi are not infrequently permanently cured. This is true even when malignant degeneration has begun. Cancroids and superficial basal celled cancers can be cured by radium irradiation with 120–150 per cent of a skin erythema dose. This produces a slight superficial ulceration that heals after an average of six weeks with a smooth scar. The results are not nearly so good in deep skin cancers reaching down to the periosteum. Tuberculous glands may be treated successfully with distant radium irradiation as well as with roentgen irradiation. The author has seen no special difference in the radium and roentgen irradiation of Basedow's disease.

The most important field for the use of radium is in malignant tumors. The immediate results have been good in tumors of the brain and hypophysis, but not much material is available in regard to late results. In tumors of the nasopharynx the Radiumhemmet at Stockholm reports 15 per cent freedom from recurrence after five years in carcinoma and 8 per cent in sarcoma. In carcinomas and sarcomas of the upper jaw, operation combined with the insertion of radium containers is the treatment of choice. The same is true of carcinomas of the lower jaw. In carcinomas of the lip in the beginning stage without gland metastases very good results are attained with radium treatment. They compare favorably with those of surgical treatment. In carcinomas of the cheek, interstitial radium treatment is used, and Quick reports 35 per cent freedom from recurrence for three years in operable cases. Cancer of the tongue in the beginning stage is one of the best fields for the use of radium needles. Cancers of the floor of the mouth are treated in the same way. Carcinomas and sarcomas of the tonsils can be treated either with needles or with cross-fire from inside and out. In sarcoma 35 per cent cure for over five years has been reported but in carcinoma only 3 to 4 per cent.

It is hard to say whether radium or roentgen treatment is to be preferred in carcinoma of the larynx. Radium irradiation has frequently been used in malignant goiter. Distant cross-fire irradiation from several fields has given good results. In inoperable cases radium irradiation has given 11 per cent freedom from symptoms for over five years; in operable cases a combina-

tion of surgery and radium has given 22 per cent. Radium treatment is particularly indicated in cancer of the breast when the skin will not tolerate any more roentgen rays. The insertion of radium needles has also been used for carcinomas of the esophagus, stomach and rectum. Radium, either alone or in combination with surgery, is extensively used in carcinoma of the uterus. It is not used in carcinoma of the ovaries except in inoperable cases as surgery gives better results, but radium gives better results than operation in cancer of the vagina and vulva: cure for more than five years in 15 per cent of the cases. Sarcomas of the extremities, sternum and ribs have been treated with radium but chiefly to avoid mutilation. Forssell reports 63 per cent five year cure with operation and radium irradiation and only 24 per cent with radium alone. Radium irradiation is particularly effective in pigmented tumors. In kidney sarcomas and hypernephromas in adults radium is used only in inoperable cases or those in which operation is contraindicated, but in cases of kidney tumor from displaced embryonic tissue in children radium treatment has proved very effective.—*Audrey G. Morgan.*

LÉVY, MAX.-M. Les variations du cholestérol chez les basedowiens traités par la radiothérapie. (The variations of cholesterol in Basedow's disease treated by radiotherapy.) *Bull. et mém. Soc. méd. d. hôp. de Par.*, Dec. 14, 1931, *55*, 1844–1846.

Epstein and Lande showed that in myxedema the blood cholesterol was elevated; in Basedow's disease it was exceptional to find the blood cholesterol above normal. Thyroid extract lowers the hypercholesterolemia of edematous nephritis. The author treated patients having elevated blood cholesterol (except edematous nephritis) by thyroxine and found that this medication, in sufficient doses, always lowered the blood cholesterol.

Nine cases of Basedow's and one normal subject were treated with roentgen rays. Total dose was 1,500 or 3,000 R; 3 to 6 sessions of 500 R each were given; 200 kv. peak, 1 mm. Cu and 0.1 mm. Al, 40 cm. distance, one field over lower anterior neck 12 cm. square. The basal metabolic rate and blood cholesterol were taken before and after treatment.

The conclusion was made: (1) that if radiotherapy in Basedow's disease lowers the B.M.R. it raises the cholesterol of the blood without there appearing to be a quantitative relationship between these two phenemona; (2) there seems to be a connection between thyroid secretion and blood cholesterol.—*Ellsworth Johnson.*

FREUND, LEOPOLD. Die Volldosen und die fraktionierte Behandlungsmethode der Karzinome. (Full doses and the fractional method of treating carcinoma.) *Acta radiol.*, Sept. 30, 1931, *12*, 315–336.

The fractional treatment was developed in Vienna in an attempt to prevent the unpleasant by-effects of large doses given in quick succession. With smaller doses at longer intervals roentgen treatment not only proved less dangerous but more effective in a number of ways. The reaction to the divided dose is not the same as to the full dose. The treatment of carcinoma with divided doses in some cases gives better results than that with full doses. The author thinks this is due to an increased selective action and the possibility of giving a greater total dose of irradiation, and also to the fact that it permits of the tumor being kept for a longer time continually in a condition of moderate reaction to the rays, so that destruction can be brought about more gradually.

He thinks the determining factors in the indications for radium and roentgen treatment of tumors are the depth at which the tumor is located, its degree of radiosensitiveness and the rapidity with which it is growing. If the tumor is growing rapidly and is very radiosensitive an intensive full deep dose should be given at one sitting in order to put a stop to the danger to the patient's life by as quick and complete destruction of the cancer tissue as possible. Tumors that are growing slowly, are not too radiosensitive nor too deep may be treated by a protracted irradiation with low doses given in rapid succession, none of the doses being below the therapeutically active dose. If the tumor is deeper but not more radiosensitive and not growing too rapidly doses of greater intensity and longer duration but with longer intervals between may be given, as it is desirable to make use not only of the more destructive action of a larger dose but also of the more selective action of the more protracted action of the rays.

For directions in regard to the technique of the fractional treatment the author refers to the publications on the subject but points out that the details must be regulated according to the individual case. He also discusses the skin reaction as a biological index.

As a means of further improving the results of treatment of cancer the author recommends using the method he has practised since 1904 whenever it is possible, namely, as radical surgical extirpation of the tumor as possible, hemostasis and roentgen or radium treatment of the open, unsutured wound.—*Audrey G. Morgan.*

Nisbet, A. T., and Keatinge, Leila, Some observations on the problem of the "erythema dose." *J. Cancer Research Com., Univ. Sydney*, 1931, *3*, 8–18.

The only justifiable dose in deep therapy is the maximum dose possible to the skin. Erythema dose is very differently defined by different authors and the standards set by Gunsett constitute an important advance, degrees of erythema being correlated with the number of r administered. Six degrees of erythema which vary with personal as well as with mechanical factors are described. There does exist a definite idiosyncrasy to radiation despite what has been said to the contrary.

Accurate voltage determination is essential as gross changes in dosage follow relatively slight voltage changes. Distribution of dosage over more than one sitting markedly increases the maximum possible erythema dose and is therefore desirable. The author uses 230 kv. with never less than 1 mm. Cu and 1 mm. Al as filters. Pelvic conditions receive 4,000 r (Solomon's iontoquantimeter) through 2 mm. of Cu through each of four ports, distributed over 21 days. Several dosimeters are discussed, none of which is entirely satisfactory.

Deep roentgen therapy is still in its infancy. New mechanical improvements are opening new fields with unlimited possibilities.—*E. W. Hall.*

Samek, J. Die Grenzstrahltherapie in der Dermatologie. (Grenz-ray therapy in dermatology.) *Strahlentherapie*, 1931, *41*, 762–766.

Bucky defined his grenz rays as the very softest roentgen rays. They produce erythema sooner than ordinary roentgen rays, and increasing the dose many times does not increase the degree of erythema. The erythema dose therefore cannot be used as the unit of dosage in grenz-ray therapy. The author is not convinced, however, of the validity of Bucky's claim that there is no danger of late injury in their use.

Grenz-ray therapy has been in use at the Prague Dermatological Clinic for about a year. The apparatus consists of small transformers which can provide a secondary tension up to a maximum of 12 kv. The tubes are incandescent cathode tubes with a water-cooled anticathode. They are of two types, differing from each other chiefly in the fact that the Müller tubes of the newer type have a considerably larger field diameter with the same focus-skin distance, which is important in general irradiation and in the irradiation of extensive dermatoses. The rays pass out through a cesium glass window of very low atomic weight covered with celluloid, called the Lindemann window, which is 0.1 mm. thick. Because of varying thickness of the Lindemann window the yield of rays varies as much as 100 per cent even with the same type of tube. Some authors say that the tubes age from the action of the weather on the Lindemann glass, but the author has not found this true in one year's use of his tubes.

The tubes used at the Prague clinic are measured every four weeks with a soft ray chamber. The half-value layer is determined partly in aluminum and partly in cellophan. The irradiation is defined by giving the number of r, the half-value layer and the focus-skin distance. It is important to keep the tension absolutely uniform, as variations in tension make more difference than they do in roentgen therapy. A tension of 11 kv. is used, 10 ma., 10 cm. focus-skin distance and 0.028 aluminum half-value layer, or for general irradiation a focus-skin distance of 15 cm. and a half-value layer of 0.03 aluminum. The average dose that causes erythema under these conditions is 300 r, though there are considerable variations. Increasing the dose five-fold only causes the same degree of erythema without exudation.

They have used this method for the local irradiation of dermatoses in about 200 cases. The individual doses varied from 100 to 1,500 r, an effort being made to keep them as low as possible. A case of follicular keratosis is described in which the nodules completely disappeared on a dosage of 500 r, though Fuhs says that 2,000 r must be used. Follicular keratosis is a special indication for grenz-ray therapy as it does not respond to roentgen irradiation. Grenz rays are also superior to roentgen rays, because of their lack of cumulative effect, in chronic recurrent dermatoses, such as chronic eczema, psoriasis and acne vulgaris. Neurodermitis is one of the best fields for the use of grenz rays, with an individual dose of not over 200 r. These rays are

particularly adapted for the treatment of the scalp as the therapeutic doses do not cause epilation. They are also adapted for irradiating organs that are very radiosensitive, as in eczema of the scrotum and anus. The author had no results in alopecia areata with doses of 300–400 r. The rays are useful in ulcerous conditions in which hard rays have a tendency to extend the ulceration. They are very effective in tuberculosis verrucosa cutis but not in lupus and scrofuloderma. In staphylococcic diseases of the skin roentgen rays are to be preferred. Purely epidermal processes are favorably affected as the grenz rays are absorbed chiefly in the epidermis. They give excellent results in the treatment of nevus flammeus with a dosage of 2,000 r. Rodent ulcers also react to this dosage.

The author has not used general irradiation with grenz rays extensively enough to be able to pass judgment on its value, though in a case of extensive psoriasis he saw retrogression of the lesions even in areas that had not been irradiated.—*Audrey G. Morgan.*

JAMIESON, R. HILLHOUSE, and HERNAMAN-JOHNSON, F. A note on the treatment of erysipelas by x-rays, with an account of three cases. *Brit. M. J.*, Jan. 10, 1931, *1*, 57–58.

The employment of roentgen therapy as an agent capable of cutting short the acute stage of erysipelas was advocated by Platau, Schlitz and Collins. The authors used a portable unit and a very small dose, repeating on consecutive days. In two cases so treated there was a fall in temperature by crisis with symptomatic relief. Protection of the hair was unnecessary due to the small doses used.—*J. H. Vastine.*

BECCHINI, GASTONE. Su due casi di rinoscleroma radium-trattati. (Two cases of rhinoscleroma treated with radium.) *Radiol. med.*, Oct., 1931, *18*, 1325–1329.

Rhinoscleroma is a specific infectious granuloma, thought to be due to an encapsulated bacillus identified by some investigators as Friedländer's bacillus. The author describes two cases in Arab women in their thirties, which he treated with radium. He preferred radium to roentgen rays because he had previously treated one case by roentgen irradiation without success. The patient was unable to stay in the hospital, however, and ambulant treatment had to be given.

In the first case he used radium puncture, as this patient had no ulcers, but in the second, in which there was ulceration, he used Columbia paste. In the first patient, after local anesthesia, he inserted 15 needles of 1 mm. platinum and containing 2 mg. radium each. The bandage was changed daily and after 240 hours of continuous irradiation the needles were removed. There was no sepsis; the points where the needles were inserted healed at once. After four months the nose was reduced to normal size and there was no interference with respiration. There was some deformity of the nose from cicatricial retraction of the soft tissues.

In the second case, a mask of Columbia paste 3 cm. thick was put on, extending down over the upper lip which was also swollen; five Dominici tubes of 2 mm. platinum containing 10 mg. radium were inserted in it. The apparatus was kept on for 480 hours, giving 20,400 milligram-hours. The apparatus was removed daily for treatment of the ulcers. Roentgen treatment was given for the enlarged lymphatic glands, as no more radium was available. The first tangible result in this case was cicatrization of the ulcers which began within fifteen or twenty days and was complete in two months, at which time there was also considerable reduction in the size of the nose. In four months the nose was normal in size and respiration normal. In this case, too, there was a certain amount of deformity from cicatrization of one of the ulcers. The lip was greatly reduced in size but not completely. A roentgenogram showed a considerable degree of repair of the superior maxilla; the enlarged lymph glands were reduced to normal. These results have persisted for a year without any signs of recurrence.—*Audrey G. Morgan.*

FRIED, CARL. Beitrag zur Bestrahlungsmethode nach Coutard. (Coutard's method of irradiation.) *Strahlentherapie*, 1931, *41*, 750–754.

Coutard has proposed a method of treatment of carinoma of the pharynx, larynx and tonsils which consists of irradiating them daily for ten to thirty days from several fields with small individual doses, strong filtration and high tension, the dose being "diluted" by strengthening the filtration and decreasing the milliamperes or increasing the distance, until one to two hours is required for the administration of 150–180 r. The effect is an extremely high total dose to the tumor and also a very considerable total surface dose to each field,

which is better borne by the skin and mucous membranes than would be expected.

The author has treated a case of carinoma of the stomach and one of carcinoma of the tongue by this method with excellent immediate results but the cases are too recent to judge the late results. The same is true of the 52 cases in which Kahlsdorf and Zuppinger have reported such good immediate results. The special point the author wishes to make, however, is that Coutard's doses varied from 5,040 to 16,200 r and similar high doses have been used in the other cases reported. But he used only 1,500 to 3,000 r primary irradiation and apparently had just as good results. His individual dose of 85 r required 19 to 26 minutes. He used a distance of 50 cm., a filtration of 0.5 mm. copper and 180 kv., diluting the dosage by using only 2 ma. He distributed the dosage over four weeks as advised by Coutard. He thinks, therefore, that the essential point in the treatment is not the thickness of the filter or the long distance and the lengthening of the irradiation time to one or two hours, but the distribution of the total dose over a period of four weeks with intervals of twenty-four to forty-eight hours between the individual doses.

He thinks caution should be exercised in giving the high dosages reported by Coutard and other authors. While the skin and mucous membranes seem to bear the irradiation well, there is as yet no proof that there will not be serious late injuries, particularly of the larynx. Another thing that will interfere with the extensive use of the method in Germany is its expense. When each patient requires several hours' irradiation a day the expense of providing the necessary apparatus is too great for small hospitals. The patients have to be hospitalized as such treatment cannot be carried on at home. The method should be tested further, but as small total doses seem to give as good early results as large ones, the smaller doses should be continued until the late results are known. If they prove less effective than the very large ones the dosages should be increased gradually until the optimum is determined.—*Audrey G. Morgan.*

Palugyay, Josef. Die Radium-Röntgentherapie des Speiseröhrenkarzinoms. (Radium-roentgen treatment of carcinoma of the esophagus.) *Strahlentherapie*, 1931, *41*, 746–749.

The few successful cases reported show that carcinoma of the esophagus can be cured by irradiation. The two most important factors in success are early treatment and proper technique. Early diagnosis is easier in carcinoma of the esophagus than in that of the stomach. In the forms with circular infiltration of the wall, which are the most favorable for radiotherapy, difficulty in swallowing occurs early. Often this is dismissed by the physician as being due merely to spasm, and sufficiently careful examination is not made. Among 56 cases of carcinoma of the esophagus which the author has seen in three years, 44 had been given roentgen examination elsewhere with negative results or a diagnosis of spasm. Carcinoma had been diagnosed before his examination in only 7 cases.

As to technique, he believes that a stomach fistula should be established in all cases in order to prevent the irritation of food passing over the tumor. The patients are apt to object to this. But as a rule the inflammation recedes, the size of the tumor decreases and much better conditions for irradiation are brought about. Even if a fistula is not established before, the reactive swelling caused by the irradiation may necessitate one. Failure may also be caused by the radium slipping out of position and by the regional glands not being irradiated. Because of the frequency of metastases in the regional glands the author believes combined roentgen and radium treatment is indicated in all cases. Local contact irradiation with radium should be given first, followed by thorough roentgen irradiation of the focus, including the regional glands. The radium capsule should always be introduced under esophagoscopic or roentgen control. The patient must be kept at rest and the position of the capsule frequently examined and corrected as it slips out of place very easily.

The roentgen and radium treatment of cancer of the esophagus requires great patience on the part of physician and patient but there are cases of cure. The author has treated 32 cases in the last ten years. Seven of the patients are still under treatment; 23 have died, 9 in the third year, 5 in the second and 8 in the first year after the beginning of treatment. In 2 of these cases autopsy did not show any local metastatic recurrence of the cancer. Two of the patients are still alive and free of recurrence one a woman of fifty-nine in whom treatment was begun four years ago and finished a year ago and one a woman of fifty-six in whom treat-

ment was begun eight years ago and finished five years ago.—*Audrey G. Morgan.*

GUISEZ, J. Présentation de malades soignés par la radiumthérapie pour cancer de l'oesophage. (Presentation of patients treated by radium for cancer of the esophagus.) *Bull. et mém. Soc. méd. de hôp. de Par.*, June 1, 1931, *55*, 908–912.

A résumé of 5 cases is given. These cases were checked roentgenographically for localization of the tumor, by the esophagoscope, and by biopsy. During the first treatments the radium is placed in position under control of the esophagoscope. Later, when the stenosis is less, the radium is put in place by sounds, in which are placed the tubes of Dominici with a sheath of 1.5 mm. platinum. The treatment lasts six or seven hours repeated every day, with sometimes one or two days' rest; a total of fifteen to twenty days' treatment is the minimum. The patients tolerate the treatments well and the results are very encouraging: swallowing becomes normal, there is gain in weight and strength, and often the patient returns to work.

The cases most favorable for radium therapy seem to be those of the middle third of the esophagus where the epithelioma is most often of the basal cell or mixed type.—*Ellsworth Johnson.*

HINTZE, ARTHUR. Unsere Fortschritte bei der Behandlung des Brustkrebses durch Nachbestrahlung. (Progress in the treatment of cancer of the breast by after-irradiation.) *Strahlentherapie*, 1931, *41*, 601–646.

The author describes the tangential method of irradiation of cancer of the breast used at the Roentgen-Radium Institute of the University Surgical Clinic of Berlin. The breast is amputated and the axillary glands cleared out, removing the pectoralis major and in some cases the pectoralis minor also. Prophylactic postoperative irradiation is then given with full doses in three series within a period of four months. As soon as the wound is healed so that dressing is not necessary, the irradiation is begun. Two fields 10×15 cm. in size are selected on the wall of the chest in such a position that their central rays, directed toward each other, are tangent to the chest wall. Similar tangential irradiations are given to fields 9×12 cm. in size in the axilla and supraclavicular fossa. Illustrations are given showing the position of the patient, the location of the fields and the incidence of the rays. It is best to begin with the supraclavicular region in order to accustom the patient to the irradiation and test her primary reaction. With this method of irradiation the lungs are not affected by the rays. The author has never seen any induration of the lungs from this method or any injury of the irradiated skin area or of the blood.

He gives graphs and tables showing the details of his results in 1,206 cases from 1912 to 1930. In 310 of these cases prophylactic irradiation was given, 417 were only operated on, 312 were irradiated for recurrence and 25 for distant metastases, making a total of 1,074 amputations. There were 22 cases operated on before 1912, making a total of 1,096 cases of amputation. In addition to this there were 104 inoperable cases treated by irradiation alone and 6 operable cases given irradiation in recent years, bringing the total number of cases up to 1,206. The tables show that the results were twice as good with operation and postoperative irradiation as with operation alone, that is, the number of patients alive after six and ten years with postoperative irradiation was as great as after three and five years with operation alone.

The physician should therefore advise postoperative irradiation. The majority of surgeons in America use irradiation before or after operation but the practice has not become common in Germany. A table is also given showing collected statistics from the world literature. In cases treated only by operation there were 28.4 per cent successful results after five years and 17.3 per cent after ten years. In cases given postoperative irradiation there were 37.9 per cent successful results after five years and 22.1 per cent after ten years, that is, the results were considerably better in the cases given postoperative irradiation.—*Audrey G. Morgan.*

ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

BY

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MAYO CLINIC

ROCHESTER, MINNESOTA

SECTION SIX

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ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

Analysis of Experimental Data

Roentgen Rays. The object of the investigations of Swann (1924) and of Stephens and Florey (1927) was to ascertain the immediate, functional effect of roentgen rays on the lungs and other organs. Swann exposed the entire body of his animals at extremely short range and observed a marked, progressive fall in blood pressure, an initial increase followed by a marked decrease in the depth and frequency of respiration, a progressive increase in tone of the cardiac muscle until contraction ceased in systole, constriction of the bronchial muscles, tonic contraction of the uterus, and increase in tone of the intestine. It is also important to note that some of the animals died after irradiation for a short time, and that death was never due to respiratory, but always to cardiac, failure. Such results would have been difficult to explain as radiation effects, especially in view of the relatively small doses of roentgen rays which the animals received. Why, for instance, should some of the animals have died so soon after a short irradiation, and why should death invariably have been due to cardiac failure? Questions such as these impelled Stephens and Florey (1927) to verify Swann's findings, which they were unable to confirm. Their studies led them to the deduction that the changes reported by Swann were not due to roentgen rays, but to high tension electrical discharges, to which the animals were exposed by their proximity to the roentgen tube. The functional disturbances described by Swann hardly seem compatible with the known action of roentgen rays, but are consistent with our knowledge of electrical effects on the body.

So far as the action of roentgen rays on pulmonary tuberculosis is concerned, the experiments of Bergonié and Tessier (1898) yielded negative results, but they furnished tangible evidence of the relative sensitiveness of the pleura and lungs to irradiation. The coexistence of tuberculous lesions may have prevented others from recognizing the relation between irradiation and the pleuropulmonary reaction described by Bergonié and Tessier, but the true significance of this feature of their experimental results did not escape them. What they apparently did not realize was the possibility that their failure to influence the tubercles in the lungs may have been due to excessive irradiation. This cannot be regarded as an established fact, but the marked inflammation of pleura and lungs which they observed is circumstantially so suggestive as to leave little doubt of its true character. If the pleuropulmonary reaction actually was an effect of irradiation, it is an unmistakable indication that the total dose of rays exceeded the limit of tolerance of the pulmonary organs. Moreover, in the light of present knowledge and experience of the action of roentgen rays on inflammatory processes, doses of this magnitude not only are less effective in causing such lesions to undergo resolution, but tend to increase the inflammation due to the specific etiologic factor by superimposing irritative, inflammatory phenomena induced by the rays themselves.

The experiments of Rudis-Jicinski (1901) are rather puzzling; judging by his report, they were crudely conceived and executed. This impression might be dissipated, however, if more complete data had been furnished. For example, it is not

clear how the acidity or alkalinity of the secretions was induced, nor indeed what these secretions may have been. All that can be said is that this investigation suggests, but does not prove, that exposure of lungs affected by tuberculosis influences the lesions favorably and apparently causes them to heal. But the rôle played by the acid or alkaline condition of the culture media or of the animal secretions is uncertain, to say the least.

The experiments of Küpferle (1913), Küpferle and Bacmeister (1913), Küpferle (1914), and Küpferle and Bacmeister (1916), apparently furnish the first tangible evidence that exposure to roentgen rays of lungs infected with tuberculosis causes, in and around the tubercles, definite changes characterized by their smaller number and size, diminished tendency to caseation, increased proliferation of connective tissue, more rapid calcification, and absence of perituberculous pneumonic inflammation; in other words, the effect of the rays is to enhance the natural tendency of such lesions to heal. These investigations were not sufficiently extensive and detailed to bring out the different histologic steps through which the alterations mentioned were brought about; but from the results of other experiments on the action of roentgen rays on tuberculosis of the skin, lymph nodes, larynx, eye, and peritoneum, as well as from what is known about the action of radiation on other forms of acute and chronic inflammation, the most logical view seems to be that the rays act first and mainly on the leucocytes (lymphocytes) infiltrating the tubercles and surrounding pulmonary tissue. Many of these cells are thereby destroyed, and the presence of cellular débris and ferments apparently leads to increased phagocytosis and also to connective tissue proliferation. If this interpretation should be substantiated, the degree of leucocytic infiltration, on the one hand, and of connective tissue proliferation, on the other, must play the leading part in the effectiveness of irradiation; another important factor should be the time relation between inoculation and irradiation. Evidence tending to confirm the significance of the last mentioned factor was furnished by Küpferle and Bacmeister, who showed that, when irradiation was begun one day after inoculation, the effect on the pulmonary tubercles was much greater than when irradiation was not started until four weeks after inoculation. Unfortunately, the number of animals used for these experiments was not sufficient to yield conclusive results.

The investigation of Manoukhin indicates that suitable irradiation of the spleen may exert on tubercles in the lungs and other organs an indirect influence quite as great as that induced by direct exposure of the infected organ. Such indirect action could occur only through the blood. In his experimental report Manoukhin did not offer any explanation, but the most logical view is that exposure of the spleen causes the destruction of the more radiosensitive leucocytes, which disintegrate and liberate in the blood their antibodies and ferments. Since the spleen contains a tremendous number of lymphocytes, which are known to be most radiosensitive and to contain lipolytic ferments, it is rational to infer that destruction of any considerable number of these cells should tend to increase the bacteriolytic power of the blood. But further experiments will be required to substantiate or to disprove the effects of indirect irradiation.

Schröder criticized Küpferle and Bacmeister for having used bacilli of human type, and employed bacilli of bovine type. The doses of culture used by him for inoculation induced extensive tuberculosis in many organs. Nevertheless, in animals

inoculated subcutaneously and irradiated, he found a distinct increase in healing of infected lymph nodes and, in the last series of rabbits in which the thorax had been exposed to larger doses of roentgen rays, the tuberculous lesions in the kidneys of the irradiated animals were fewer in number and smaller than those in the unirradiated, control animals; but the pulmonary lesions did not differ perceptibly. The discrepancy between the results obtained by Küpferle and Bacmeister and those of Schröder may perhaps be accounted for by difference in virulence of the organisms employed or, as suggested by Schröder, by variation in resistance of the rabbits to bacilli of the human and bovine types; but the dose of culture injected, the time after inoculation at which irradiation was started, the frequency of exposure, and the dose of rays also may have been factors the significance of which cannot be appraised for lack of specific data. Gorke and Töppich also were unable to observe any effect of roentgen rays on tuberculosis of the lungs.

Numerically, the negative reports are as strong as the positive reports, and there is no reason why one group should be accepted and the other rejected. Yet the fact that experienced investigators should have found that, under certain conditions, exposure to roentgen rays does influence tuberculous lesions in the lungs makes one wonder if the inability of others to obtain similar effects may not have been due to variations in technique. Schröder's criticism that rabbits have a strong natural resistance to bacilli of human type and that the apparent influence of irradiation, shown by Küpferle and Bacmeister, was probably due to this fact does not appear strong. The resistance of rabbits to human bacilli must be admitted, but to use the more virulent, bovine type of organism does not improve the quality of the experiment, because the resulting disease is so active and generalized that the rays may be powerless to influence its relatively short course. Schröder's inability to observe any influence of irradiation, therefore, does not necessarily prove that the effects previously reported by Küpferle and Bacmeister were not results of irradiation. Although the influence of roentgen rays on tuberculosis of the lungs cannot be said to be absolutely established, it is probable that the rays exert a definite but limited action on lesions of which leucocytic infiltration is a more or less prominent feature.

The investigations of Bergonié and Tessier (1898), Wohlauer (1909), Küpferle and Bacmeister (1916), Warren and Whipple (1922), Davis (1924), Tsuzuki (1926), Hartman, Bolliger, Doub, and Smith (1927), Warthin and Pohle (1929), and Lüdin and Werthemann (1930) all relate to the specific radiosensitiveness of the lungs and pleura and show that, within certain limits of dosage, roentgen irradiation is well tolerated, while exposure beyond such limits may cause more or less severe or extensive inflammation of the pleura and lungs. The experiments of Bergonié and Tessier (1898) related primarily to the influence of roentgen rays on tuberculosis of the pleura and lungs induced experimentally; this phase has been discussed elsewhere (page 115). They are mentioned here because, although Bergonié and Tessier found that irradiation under the conditions of their experiments did not prevent or modify the evolution of tuberculous lesions resulting from artificial inoculation, they found that exposure of the lungs to sufficiently large doses of roentgen rays may incite the pleural and pulmonary tissues to inflammatory reaction. Moreover, they realized that the inflammation, which took the form of marked proliferative thickening of the pleura and extensive symphysis of the visceral and parietal layers of this membrane, was not related to the tuberculous process, but represented a direct effect of

the rays. This observation of chronic proliferative and adhesive pleuritis undoubtedly represents the first clear example of the specific radiosensitiveness of the pleura. The fact that they did not observe corresponding reaction of the pulmonary parenchyma may merely mean that they could not distinguish such irritative inflammation from that incidental to the tuberculous process, especially since the tissues were not examined microscopically. If the lungs themselves had been submitted to microscopic examination, it is likely that corresponding abnormalities would have been found. Such pronounced inflammation of the pleura by itself is a sufficient indication that the total dose of radiation given by Bergonié and Tessier was relatively large. There can be no doubt that the pleuritis was a direct effect of the rays, because reactive inflammation was noted in all the irradiated animals, but never in those inoculated with tubercle bacilli at the same time and in the same manner but not exposed to roentgen rays. The experiments of Küpferle and Bacmeister (1916) also related primarily to the action of roentgen rays on pulmonary tuberculosis. Unlike Bergonié and Tessier and under different experimental conditions, they found that irradiation had a substantial influence on the pulmonary tubercles which were fewer in number and smaller and which showed a much greater tendency to repair. In their third series of rabbits, in which the animals were exposed to the largest doses of radiation, the lungs of all but one of the irradiated animals presented evidence of extensive and acute bronchitis and pneumonia. Moreover, the degree of bronchial and pneumonic inflammation was proportional to the dose to which the thorax of each animal had been exposed; the single rabbit in which such disturbances were not found was that which had received the smallest dose. Küpferle and Bacmeister also realized the significance of this observation and rightly attributed it to excessive irradiation.

The first impression derived from the investigations of Wohlauer (1909) is that the pathologic modifications noted represented actual, direct injury to the lungs, but a careful review makes one doubt such relationship. The lungs of animals that had received small doses showed changes similar to those of animals that had received doses many times greater. Moreover, the character of the abnormalities suggests the possibility that they were partly due to the action of the rays on other structures. Lack of precise information about the anatomic limits and dimensions of the field of irradiation, in those animals in which an attempt was made to confine the action of the rays to the intrathoracic structures, and also about the condition of the abdominal organs, renders final analysis impossible. Certain suggestive points, however, attract attention. Clinical disturbances in the first animal, the entire body of which had been exposed to a dose of roentgen rays seven and one-half times greater than the limit of tolerance of the skin, appeared five days later, and death ensued within two days. The second animal (thorax only), which had received five times an erythema skin dose in two successive days, died one day after the second irradiation. The pathologic changes in the lungs of these two representative animals varied only in degree. These changes included hyperemia, alveolar exudation, dilatation of the peribronchial and perivascular lymph spaces, infiltration of these spaces with erythrocytes and leucocytes, and the first animal also presented innumerable punctate hemorrhages. The lungs of the third animal, whose thorax had received approximately the same dose as that of the second animal, showed only slight capillary hyperemia and enlarged lymph nodes. If such abnormalities had

been a direct and specific effect of roentgen rays on the lungs, they probably would not have appeared so soon as one day following exposure (second animal), and their degree should have corresponded more closely to the dose. With the information available we can only surmise that, while the intention may have been to irradiate only the thoracic organs, the field of exposure probably was sufficiently large to include some of the structures below the diaphragm, such as the spleen and upper portion of the small intestine. Attention must also be called to the undoubted influence of the rays on lymph nodes in the mediastinum and in the lungs themselves, but this would not seem sufficient to cause death. As we shall see when the experiments of Tsuzuki are considered, similar pulmonary abnormalities occurred in almost all his animals, but these changes were only temporary and disappeared when the animals survived long enough. The foregoing interpretation is strengthened further by the inability of Warren and Whipple to find any pulmonary changes when irradiation was really confined to the part of the thorax corresponding to the lungs. Warren and Whipple did not find any abnormalities in these organs, probably because the doses of roentgen rays which their animals received were within the limit of tolerance of the pleuro-pulmonary structures. Davis, on the contrary, obtained unmistakable evidence of inflammatory reaction in the pleura and lungs. The conditions of irradiation and dosage were admittedly severe and calculated to produce reaction. Davis gave his animals large doses several times at short or long intervals; considering the size of the animals, such doses were much larger than those used in treating human beings. He was not trying to determine the limit of tolerance of the lungs and pleura, but rather the character of the lesions induced by excessive doses. Such reaction was characterized by weakness, loss of weight, dyspnea, fever, serofibrinous pleuritis and pericarditis, edema, exudation, and epithelial desquamation, followed by thickening of the alveolar walls, reduction in size or obliteration of the air spaces, interalveolar hyperemia, increase in connective tissue around the bronchi and blood vessels, and marked thickening of the blood vessels themselves.

Tsuzuki also noted, in the lungs of his animals, hyperemia, edema, serous or hemorrhagic exudation in the alveoli, desquamation of some of the alveolar and bronchial epithelium, and degeneration or destruction of lymphocytes and phagocytosis in the peribronchial tissues, but these abnormalities disappeared after from twenty-four to seventy-two hours, except in the animals which were irradiated continuously until death. The early appearance of these changes and their subsequent disappearance make it seem probable that they resulted from the extensive cellular degeneration in other organs and tissues found and described by Tsuzuki, and not from direct and specific action of the rays on the lungs. Attention may be drawn to one possible exception. The degeneration and phagocytosis of lymphocytes in the peribronchial tissues may well have been a direct effect of irradiation, unless these cells were injured while circulating in the blood stream and were carried to the lungs. There is ample proof of the great vulnerability of lymphocytes and lymphoid tissues generally. In any event, the difference between the findings of Davis and of Tsuzuki merely reflects the difference in dosage and in the method of irradiation.

When the experimental data given by Hartman, Bolliger, Doub, and Smith are reviewed, it is found that their animals received doses five to eighteen times larger than those given to human beings, because their primary object was to find an

experimental method of inducing chronic myocarditis. That they were successful is not surprising under the circumstances, but their interpretation of the mode of action of the rays is open to question. Although irradiation was directed principally to the heart, the size of the field exposed to the rays was sufficiently large to include a portion of the lungs. Moreover, the intensity of irradiation is roughly indicated by epilation and frequent ulceration of the skin and by passive hyperemia and edema of the exposed thoracic tissues. While the resulting cardiac abnormalities were stressed, it is important to note that the lungs also suffered considerably. As was pointed out in considering the action of radiation on the heart, it is probable that some of the pathologic changes in the pericardium and heart were secondary to the acute pleuropulmonary inflammation. It is likely, however, that other cardiac alterations, notably the thickening or obliteration of the blood vessels, may have constituted late signs of direct injury by irradiation, but their experiments did not establish conclusively that the hyperemia, myocardial degeneration and leucocytic infiltration were specific effects of the rays. But there can hardly be any doubt that the acute and chronic inflammation in pleura and lungs was a direct result of irradiation.

In this connection it is interesting to scrutinize the experiments of Warthin and Pohle (1929). They used rats and rabbits and gave to the precordial region and mediastinum one human erythema dose of roentgen rays of medium and short wavelength, followed by one-half the human erythema dose on two subsequent occasions at intervals of one month. It must be obvious that to give to a rat or rabbit a dose which represents the maximum for a body the size of a human being is to give the animal a dose several times larger in proportion to its size. And to repeat even half such a dose in one month is to test the tolerance of the animal to or beyond the limit. As in their previous investigations (1927) on the influence of roentgen rays on the heart, Warthin and Pohle again found hyaline and fatty degeneration, Zenker's necrosis, and inflammatory reaction of the myocardium, but these were now complicated by catarrhal or purulent bronchitis and bronchopneumonia affecting the large bronchi and the portions of the lungs in the anterior mediastinum. A remarkable thing, however, was that pulmonary and myocardial lesions of the same character, though less severe, were found in the majority of the unirradiated, control animals. Because the myocardial and pulmonary abnormalities were less pronounced in the control than in the exposed animals, Warthin and Pohle felt that the cardiac lesions were at least partly due to irradiation which primarily injured the heart, large bronchi, and portions of the lungs, and that a secondary, infective bronchitis and bronchopneumonia extended to the pleura, mediastinum, and pericardium. In view of the results of their earlier experiments, it would seem even more probable that the strong doses of rays irritated the more sensitive pleura and lungs rather than the less sensitive heart, that the inflammatory reaction of the pleura and lungs extended by continuity to the pericardium and epicardium, but that the degenerative alterations in the myocardium were mainly the result of circulatory, toxic factors only indirectly related to irradiation. The incidence of similar, though less marked, changes in their unirradiated, control animals points to infection transmitted from the irradiated animals through infected exudates. This assumption, made by Warthin and Pohle themselves, is undoubtedly sound and is strengthened by their observation that, in animals that had not been exposed to the rays, the

respiratory infection was less pronounced; this probably meant that, in these animals, the infection occurred later than in the irradiated rabbits.

Among the epithelial cells that line the bronchi and their larger, intrapulmonary branches are cells which have the property of secreting mucus; the mucosa of the larger bronchi also contains mucous glands. This circumstance may have an important bearing on the effect of irradiation on the lung because, as has been pointed out in connection with the influence of roentgen rays and radium on the salivary glands and intestine,[168] epithelial cells which secrete mucus are much more susceptible to the rays than ordinary epithelial cells. There is reason to think, therefore, that the mucus-secreting cells of the bronchial mucosa and of the mucous glands are equally sensitive. If this assumption is well founded, just as in the gastrointestinal epithelium mucoid degeneration of the mucus-producing cells of the bronchi and their mucous glands should be an early step, if not the first step, in pulmonary reaction to irradiation. The only clue to such mucoid degeneration, given by any of the foregoing investigators, is the catarrhal bronchitis affecting the large bronchi and portions of the lungs in the anterior mediastinum, mentioned by Warthin and Pohle. But the fact that bronchitis often had become purulent in character and was accompanied by bronchopneumonia diminishes the possible significance of the clue. At any rate, the reactive inflammation was so intense that it is impossible to distinguish the order of reaction of the different pulmonary tissues. Catarrhal, mucous or purulent secretion is a common feature of bronchitis from any cause, and the relationship of the catarrhal and purulent bronchial secretion to irradiation, noted by Warthin and Pohle, must therefore remain uncertain. The results obtained by Lüdin and Werthemann (1930) closely resemble those described by Warthin and Pohle, and in general the effects described were so similar that the factors involved in their production were probably identical. Here again, pleuropulmonary inflammation, with focal, coalescing, bronchopneumonia, appears to have been the initial and direct result of irradiation. Whether or not the degeneration and desquamation of the alveolar and bronchial epithelium, and the mucous or mucopurulent bronchitis also, are to be regarded as direct effects of irradiation is not certain. As in the intestine and salivary glands, exposure of the lungs to the rays may cause the mucus-producing cells in the larger bronchi to undergo mucoid degeneration, but these experiments do not furnish clear evidence on this point. On the whole, it seems probable that the alveolitis, bronchiolitis, and bronchitis are a part of the primary, direct effect of irradiation. The cardiac alterations found by Lüdin and Werthemann, on the other hand, appear to have been indirect rather than direct effects of the rays; such pathologic changes were probably caused by the circulation of toxic products arising primarily in the injured pleura and lungs as well as in the blood circulating through the irradiated territory.

Radium. The experimental studies of Pappenheim and Plesch (1913) and Lazarus-Barlow (1922) furnish a striking illustration of the extensive abnormalities caused by exposing the entire body to sufficient doses of radiation, either by internal administration (Pappenheim and Plesch) or by external irradiation (Lazarus-Barlow). They also give additional evidence of the extraordinary sensitiveness of leucocytes, especially lymphocytes, in the blood, spleen, lymph nodes and bone marrow. The

[168] See Action of Roentgen Rays and Radium on the Gastrointestinal Tract, Am. J. Roentgenol. & Rad. Therapy, 1931, *26*, 145, 335, 493.

destruction of lymphocytes, indeed, was the most salient feature of the changes observed. The abnormalities described by Pappenheim and Plesch included degeneration of the endothelial cells lining the blood vessels, with hemorrhage into the surrounding tissues, and more or less profound cellular degeneration, hyperemia, and multiple hemorrhages in the parenchyma of many organs, including the liver, kidney, lung, heart, stomach and intestine, and testis or ovary. Most of these changes appear to have been secondary to the circulation of toxic products of cellular disintegration in the more sensitive organs and tissues. There is no good reason for believing that, aside from destruction of lymphocytes and injury to the vascular endothelium with subsequent thickening of the wall of the vessels, the pathologic changes in the lungs represent a specific and direct injury by the rays. The difference in the action on various organs between internal and external irradiation is not great and may be accounted for by a difference in the quantity of radiation reaching the cells of the different organs. It seems probable that the time during which the radioactive substance was held in each organ, or the time required by each organ to dispose of it, may have been the most important factor in the alterations produced. A noteworthy point brought out by Pappenheim and Plesch was that, except for the destruction of leucocytes in the blood, spleen, lymph nodes, and bone marrow, intravenous injection of thorium X had the greatest effect on the liver, while the kidneys and large intestine sustained the major abnormalities after oral administration. As has been shown elsewhere,[168] thorium X appears to be excreted chiefly through the kidneys and large bowel, and the extreme hyperemia and edema of the former and the epithelial ulceration of the latter, noted in these experiments, undoubtedly have a similar meaning. The reason for the more profound degenerative changes in the liver after intravenous injection, however, is not so obvious.

Clinical Considerations

Radiotherapy for Pneumonia. Impressed by remarkable metabolic changes which they had found in patients with leukemia treated with roentgen rays, MUSSER and EDSALL (1905) suggested the possible advantage of such treatment for unresolved pneumonia. They reported one case in which roentgen irradiation was followed by rapid resolution and improvement, but stressed the point that such an effect could not be expected after organization had occurred. EDSALL and PEMBERTON (1906) cited three additional cases of delayed pneumonic resolution, in which moderate irradiation of the lungs promptly initiated resolution, with correspondingly striking subsidence of the clinical manifestations. They held that the treatment could not be effective after organization and considered active, continued inflammation, with fever and toxemia, and tuberculosis, as contraindications. At that time ferments occupied an excessively important place in biologic and medical thought, and Edsall and Pemberton expressed the idea that the rays acted on the pneumonic process by accelerating the action of ferments and stimulating autolysis, but they admitted the "widespread and excited tendency to give ferments a more important place than is their due." A noteworthy feature of their studies was the observation that the excretion of nitrogen increased sharply after each exposure to small doses of roentgen rays.

For some reason the remarkable influence of roentgen rays on delayed resolution

in pneumonia, revealed by such well-known clinicians, remained unutilized for ten years, when QUIMBY and QUIMBY (1916) confirmed the experience of Musser, Edsall, and Pemberton in twelve cases of delayed resolution, only four of which were described in some detail. Although resolution had been delayed for some time, it progressed rapidly after roentgen irradiation of the lungs, and the patients promptly recovered. One eleven-year old boy aspirated a tooth and developed pneumonia, which threatened serious consequences but which responded quickly to treatment. Another favorable result was obtained in a ten-year old boy, who developed pneumonia after a crushing injury to the thorax. So gratifying were the results that Quimby and Quimby were prompted to remark that "no pathologic process in the body responds quicker to an X-ray exposure than the non-resolution following pneumonia." They attributed this effect of roentgen rays to destruction of leucocytes infiltrating the lungs. KROST (1925) supplemented the foregoing reports by adding twelve more cases, in eleven of which irradiation of the thorax led to improvement in symptoms and rapid recovery. The posterior aspect of the thorax of his patients was exposed for five minutes to rays generated at a potential equivalent to a $7\frac{1}{2}$ inch spark-gap, filtered through 3 millimeters of aluminium and 4 millimeters of sole leather, with 5 milliamperes of current, at a focal-skin distance of 8 inches. Only two patients required a second exposure ten days or two weeks later. Krost thought irradiation stimulated phagocytosis. Additional evidence of the resolving action of roentgen rays on pneumonic exudates has been furnished by Torrey (1927). MERRITT and MCPEAK (1930) reported seven additional cases of unresolved pneumonia, in four of which a single irradiation of the affected pulmonary parenchyma was followed by prompt and complete resolution of the inflammatory process. In two other cases the hilar lymph nodes and part of the parenchyma of one lung were inflamed. Irradiation brought distinct improvement; the parenchymatous infiltration yielded rapidly and the hilar adenitis more slowly. In the remaining patient, a man aged seventy-five years with a pulmonary lesion of uncertain character, the rays did not have any apparent effect.

HEIDENHAIN (1917) claimed that small doses of roentgen rays also had a favorable influence on postoperative pneumonia. He recorded forty-eight cases, in over 80 per cent of which the course of the disease was said to have been shortened. He described one case, in which the normal instead of the diseased lung was accidentally irradiated and in which the pulmonary inflammation cleared up and the condition of the patient improved as rapidly as in those in which the affected lung was exposed to the rays. Heidenhain deduced that the influence of the rays could hardly represent a local effect. He obtained equally favorable results in over 50 per cent of twenty-four cases of pneumonia unrelated to surgical intervention. In two of these resolution was delayed but yielded rapidly to treatment. HEIDENHAIN and FRIED (1924) gave their results in fifteen cases of postoperative pneumonia and five cases of acute or chronic pleuritis. Ten to 20 per cent of the erythema skin dose was given to the thorax. The pneumonic process abated rapidly in nine of the postoperative cases, and in four of the five cases of pleuritis fever and other symptoms subsided in an unusually short time. No attempt was made to explain how the rays brought about the changes observed. The results obtained by KAESS (1925), in ten patients with bronchopneumonia, were equally satisfactory; the inflammatory process subsided promptly in eight cases, but proved refractory to treatment in two cases of

bronchopneumonia and in one case of lobar pneumonia. FRIED (1926) reported successful results in thirty-two of a series of forty cases of postoperative pneumonia, and in five other patients with bronchial or lobar pneumonia, who had not been operated on. The lungs were exposed, through one large field, to doses varying between 80 and 200 R[169] of roentgen rays generated at a potential of 140 kilovolts and filtered through 0.5 millimeter of zinc and 0.5 millimeter of aluminium. Without citing any actual examples, HOLZKNECHT (1926) wrote that among the many cases of bacterial infection and suppuration in which he had tried roentgen therapy with success were many cases of postoperative pneumonia; in one-third of these, the course of the inflammatory disturbance had subsided by crisis, and in another third by lysis. Only from 10 to 20 per cent of an erythema dose had been directed to the area of consolidation or infiltration. GADJANSKI (1927) also testified to the excellent therapeutic effect of small doses of roentgen rays in more than forty patients, most of whom suffered from pneumonia as a sequel of influenza. GLAS (1927) reported excellent results in fifty-seven cases of pneumonia, pleuritis, and bronchitis. Great improvement, with return to normal temperature within two or three days after irradiation, was noted in thirty-nine patients (68 per cent); in two the fever subsided six and ten days, respectively, after irradiation; in five the pulmonary condition improved, but continued fever indicated residual or latent disturbances; the condition of three patients improved after each exposure to the rays, but repeated exacerbations of pulmonary inflammation developed; and, in spite of irradiation, eight patients died from multiple abscesses, gangrene, subphrenic abscess, etc. In 1928, FRIED recorded a total series of fifty-seven patients suffering from bronchopneumonia, in over 80 per cent of which rapid recovery followed roentgen irradiation of the lungs; fourteen of these patients were children. BOTHNER (1928) described seven cases of bronchopneumonia in infants. The thorax was exposed to 10 per cent of the skin tolerance dose of rays filtered through 0.5 mm. of zinc and 1 mm. of aluminium. When the disease was not severe resolution appeared to be hastened, but when the pneumonitis was pronounced the rays did not seem to influence it appreciably. It has often been noticed that, during infancy, inflammatory processes do not respond so favorably to irradiation as similar conditions in adolescents or adults. HOLTZ (1929), who had treated thirty-three cases of croupous and bronchopneumonia, wrote that irradiation diminishes the severity and shortens the course of the inflammatory process. He stressed the importance of early treatment and used doses of from 15 to 18 per cent H.E.D., after fluoroscopic examination to determine the extent of the area to be exposed. HELL (1929), however, was not so successful. He treated twenty-four cases of pneumonia, in some of which the pulmonary infection followed a surgical intervention. Favorable results were noted in only three instances, and the data furnished are insufficient to explain the discrepancy between his failure and the success of so many others.

As previously mentioned, Musser and Edsall and Edsall and Pemberton thought the action of roentgen rays on delayed resolution was to stimulate autolysis by increasing the activity of ferments. Quimby and Quimby ascribed the distinct influence of irradiation on resolution to destruction of infiltrating leucocytes. Heidenhain did not offer any explanation, but described one case, in which equally favorable results followed accidental irradiation of the normal instead of the diseased

[169] German Roentgen.

lung. Krost expressed the opinion that the rays stimulated phagocytosis. These various interpretations appear more divergent than they really are. Although absolute proof is lacking, it seems probable that the activation in ferment action and autolysis invoked by Musser, Edsall, and Pemberton, the destruction of infiltrating leucocytes mentioned by Quimby and Quimby, and by Pordes, and the increase in phagocytosis referred to by Krost, represent only different phases of the same effect. Ample evidence of the exceptional susceptibility of leucocytes, especially the lymphocytes, to irradiation will be presented elsewhere. This evidence shows that leucocytes are rapidly destroyed by small doses of radiation and that the products of such destruction are removed mainly by phagocytosis, but perhaps also by other means the nature of which is not yet clear. The rapidity of response to irradiation suggests that the first and chief effect is on the lymphocytes infiltrating the pneumonic lesions as well as lymphocytes circulating in the pulmonary vessels, from which the protective substances and certain ferments are thereby liberated and rendered more effective for defense. This would explain the increase in phagocytosis and autolysis, and the failure of irradiation after the onset of organization. But this explanation does not appear to cover the rapid resolution of the pneumonic process in the lung of one patient, in whom irradiation had accidentally been directed to the opposite, normal lung. It is possible that more detailed information about the precise method of irradiation in this instance might furnish an adequate solution; under the circumstances, any attempt to analyze the factors involved must be based on conjecture. Nevertheless, since lymphocytes and other varieties of leucocyte in the circulating blood are known to be destroyed by irradiation, it is probable that exposure of the uninflamed lung to roentgen rays also results in appreciable destruction of such cells, from which antibodies and ferments are liberated in the blood stream and may influence the inflammatory lesions in the affected lung.

Radiotherapy for Whooping Cough. At the instance of a physician, whose child had whooping cough and who was aware of the therapeutic value of irradiation in hyperplastic enlargement of the thymus gland in children, LEONARD (1924) agreed to give a small dose of roentgen rays to test their effect. Accordingly, the anterior and posterior aspects of the thorax and neck were exposed alternately, every second day, to rays generated at a potential equivalent to a spark-gap of 15 cm., filtered through 1 mm. of aluminium, at a focal-skin distance of 35 cm, and each field received 5 ma. for 4 minutes. The anterior surface of the thorax received this dose twice, and the posterior surface once only, but this was sufficient to cause a strikingly favorable change in the child's condition. Whereupon, Leonard treated fifty other cases in which a definite diagnosis of whooping cough had been made. The results were sufficiently good to induce him to present them to the staff of the Boston Floating Hospital, which provided the funds and facilities necessary to test the method more thoroughly. This was done in about four hundred cases, on which careful clinical, roentgenologic and bacteriologic studies were made. Enlarged tracheobronchial lymph nodes were found in most of the cases, and such enlargement was regarded as greater than that found in measles, scarlet fever, or diphtheria. The lymphadenopathy appeared most pronounced during the third week of the disease. As in the first instance, the patients were irradiated from two to four times every second day. In at least 75 per cent of the patients treated during the paroxysmal stage of the disease the symptoms were relieved; in children less than one year old,

relief was obtained in almost every case. The outstanding and earliest effect of treatment was cessation of vomiting, and the frequency and severity of the paroxysms diminished. The duration of the disease did not appear to be greatly altered, and too early treatment did not prevent paroxysms.

BOWDITCH and LEONARD (1923) issued a preliminary report based on twenty-six cases between three months and forty years of age. The thorax of each patient was exposed three or four times at intervals of two or three days, and the total dose was "well under an erythema dose." In a small percentage the treatment was followed by prompt relief; the whooping and paroxysms quickly disappeared. Seventy per cent improved to the extent that the paroxysms diminished greatly in frequency and severity. In 10 or 15 per cent of the patients, the treatment had no apparent influence on the disease. Impelled by the report of Bowditch and Leonard, KINGSTON and FABER (1923) tested this method of treatment in twenty-four patients between seven months and thirteen years of age, in all stages of whooping cough. Through large anterior and posterior thoracic fields, they gave one-fourth of an erythema dose of roentgen rays[170] from one to three times at weekly intervals. Remarkable improvement after a single exposure was noted in four cases. In ten patients, the vomiting and paroxysms stopped after two exposures. Eight others improved gradually, but were not cured; and two patients were not relieved, even after three exposures. Kingston and Faber also mentioned cessation of vomiting as the earliest and most salient result of treatment. Six additional cases, in which cough and vomiting ceased after two or three exposures of the mediastinum to from one to two and one-half Hozknecht units at intervals of four or five days, were reported by BONER (1924). He also thought this due to the action of the rays on enlarged tracheobronchial lymph nodes.

On the basis of three hundred patients from a few weeks to fifty years old, all of whom had paroxysmal cough and whooping and most of whom also presented cyanosis and vomiting, BOWDITCH (1924) stated that over 80 per cent were benefited. The thorax was irradiated[171] three or four times, on alternate days, and this was repeated one or two weeks later when the disease resisted treatment. The dose given in three or four exposures totaled less than half an erythema dose. The patients noted improvement within a few hours, and the paroxysms diminished in frequency and severity. The change was greatest after the third exposure, when noticeable relief, abatement of paroxysms, vomiting and cyanosis, and cessation of whooping occurred. Only one patient died. BOWDITCH, LEONARD, and SMITH (1924) analyzed twenty carefully studied cases of whooping cough, in eighteen of which the patients were not more than three years old, and seventeen of which were in the first three weeks of the disease, as far as symptoms were concerned. Preliminary blood counts showed an initial lymphocytosis which attained its maximum in the third week. Enlargement of tracheobronchial lymph nodes and marked peribronchial thickening of the larger bronchi, especially in the lower lobe of the right lung, were commonly found. Definite infiltration of the right lower lobe, probably bronchopneumonic in character but without clinical manifestations, was observed in 30 per cent of the

[170] Rays generated at a potential equivalent to a spark-gap of $9\frac{3}{4}$ inches, filtered through 0.25 mm. of copper at a focal-skin distance of 12 inches; 5 ma. of current for 4 minutes.

[171] Rays generated at a potential equivalent to a spark-gap of 15 to 17.5 cm., filtered through 1 mm. Al, at a focal skin distance of 70 cm. (?); the anterior and posterior aspects of the thorax each received 4 ma. for from 3 to 5 minutes, according to the age of the patient.

patients. The treatment caused the paroxysms to diminish in number and intensity from an average of about fourteen per day, five days after the initiation of treatment, to two per day after two weeks, and this was accompanied by a fall in the number of leucocytes. Three cases, in which whooping cough was complicated by bronchopneumonia, derived as much benefit as the others. In some of the patients, the entire chest, and in others only the root of the lungs, was exposed three times from front and back, at a focal-skin distance of 16 or 18 inches, to a total of approximately two-thirds of an erythema dose.

Additional evidence of the supposed therapeutic value of roentgen rays in whooping cough was furnished by STRUTHERS (1924), whose communication included forty-five cases in patients from three months to thirty years of age, in which paroxysms had been present for from two days to eight weeks. All but one had the clinical features characteristic of pertussis. A single irradiation was given to each patient, and only seven or eight patients received medicinal treatment in addition. Seven cases were classed as "prompt cures," because the whooping and vomiting stopped within twenty-four or forty-eight hours, although a slight morning cough persisted two weeks longer. The symptoms of twenty patients were considerably relieved in four or five days, while in eighteen others the treatment proved useless. SMITH and KIRBY (1924) added twenty more cases, in which they claimed that exposure of the thorax to less than one erythema dose of roentgen rays yielded favorable results. BOWDITCH and SMITH (1925) published an extensive report of their results in over 850 cases, and expressed their conviction that "roentgen ray treatment is the most uniformly satisfactory means of treating whooping cough." Irradiation was said to be most effective during the paroxysmal stage, and infants were thought to derive the earliest and greatest benefit. Treatment during the catarrhal stage did not modify the course of the disease. Immediate improvement was noted in over 70 per cent of the cases, and this was accompanied by a fall in the number of leucocytes and in the percentage of lymphocytes. In another analysis of the same cases, SMITH, BOWDITCH, LEONARD, et al (1925) explained that the patients had been divided into two groups, one group being treated with roentgen rays alone, and the other with roentgen rays and vaccines combined. It was their impression that the combined treatment yielded the most favorable results. A definite reduction in size of the hilar nodes and diminution of peribronchial thickening were found in both groups by the end of the second week, and often by the end of the first week. Only three of the patients died. Their extensive experience and findings were thought to prove the value of radiotherapy in reducing the number and intensity of the paroxysms and in shortening the duration of the disease. Other reports testifying to the value of roentgen-ray treatment for pertussis have been made by DE PUELLES (1924), FRIEDMAN (1925), PINCHERLE (1925), PINOS and PUYADAS (1926), HRABOVSKY (1926), GERBER (1927), and others, but each of these was based on a comparatively small number of cases.

By the number of patients on which they were based and by the details given, the foregoing reports appear quite convincing. But scientific records of the treatment of pertussis are known to contain a multitude of reports of the remarkable therapeutic effect of vaccines, various forms of medication, ultraviolet light and other methods. Each has had its vogue and has been discarded or has passed into relative discredit. In this connection the report of FABER and STRUBLE (1925) is of more than passing

interest. Assuming that roentgen-ray treatment for pertussis possessed real value, they undertook to study a series of forty-four cases in the paroxysmal stage of the disease. The diagnosis was based on the symptoms and the blood count. A daily record of paroxysms and vomiting was kept, and the patients were carefully watched during, and for a time after, the treatment. Twenty-two of these were treated with roentgen rays,[172] and twenty-two others were not irradiated but were given antipyrin. Parallel curves of the twenty-two irradiated and twenty-two unirradiated cases revealed that the patients who had not been exposed made a better showing in all respects than those who had been exposed to roentgen rays. The curves also disclosed that, in general, roentgen-ray treatment had been given during the period of natural decline of symptoms. Faber and Struble stressed the point that the mothers' statements about the effect of treatment were found untrustworthy. In some of the patients who had not been irradiated, the number and severity of the paroxysms diminished as rapidly as in some of the treated patients. The inevitable conclusion was that roentgen rays do not have any curative or beneficial effect on whooping cough.

Because they had observed marked enlargement of tracheobronchial lymph nodes and so-called peribronchial thickening and infiltration of the lower lobe of the right lung during the second or third week of the disease, and because these abnormalities diminished or disappeared after the patients' thorax had been exposed to the rays, Leonard, Bowditch, Smith, and their associates, inferred that the ensuing relief from symptoms was a manifestation of action of the rays on the lymphoid elements of the mediastinal nodes and possibly also of the thymus gland. Boner, and Smith and Kirby also, held the same view. Gerber felt that the rays diminished the sensibility of the vagus nerve endings. If the therapeutic value of irradiation in whooping cough had not received such sharp contradiction from the work of Faber and Struble, the assumption, by Leonard, Bowditch, and Smith, by Boner, and by Smith and Kirby, of an action of roentgen rays on lymphoid elements in the mediastinal nodes must have been accepted as the only plausible explanation of the clinical changes observed. The nature and rapidity of such changes and the small doses of radiation by which they appeared to be produced would be consistent with the exceptional radiosensitiveness of lymphoid cells. This interpretation would also be supported by the decrease in the number of leucocytes after irradiation had not the studies of Faber and Struble apparently shattered this hypothesis by indicating that the improvement in symptoms, the reduction in size of the tracheobronchial lymph nodes, and the smaller number of leucocytes in the circulating blood probably were incidents in the natural course of the disease and not results of irradiation. It is true that the number of cases observed by Faber and Struble was small, and that more extensive investigation of the problem would be desirable. Nevertheless, it seems fair to conclude that the therapeutic value of roentgen irradiation in pertussis is uncertain and at the present time stands unproved.

[172] Six-inch fields over the anterior and posterior aspects of the thorax were exposed to rays generated at a potential equivalent to a spark-gap of 9 inches, filtered through 0.25 mm. of copper and 1 mm. of aluminium, at a focal-skin distance of 12 inches. Three patients less than fifteen months old received 8 ma. for one minute (56 E units); two patients between fifteen and twenty-four months received 8 ma. for two minutes (112 E); and seventeen patients over two years old received 8 ma. for three minutes (168 E). They were all treated three times at intervals of three or four days.

To be Continued.

WILLIAM A. EVANS

President of the American Roentgen Ray Society

1932–1933